Molecular genetics of abdominal aortic aneurysm

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Statement of originality

The work contained in this thesis is my own original work, except where

acknowledged in the text.

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TABLE OF CONTENTS

LIST OF ABBREVIATIONS

A 260/280	Ratio of absorbance of RNA at 260 and 280 nm
AAA	Abdominal aortic aneurysm
ACE	Angiotensin converting enzyme
ADAM	A disintegrin and metallopeptidase
AHCY	Adenosylhomocysteine
ALK	Anaplastic lymphoma receptor tyrosine kinase
Apo	Apolipoprotein
AOD	Aortic occlusive disease
BAI-1	Brain specific angiogenesis inhibitor 1
BTG-2	B – cell translocation gene - 2
DNA	Deoxyribonucleic acid
CCR3	C – C chemokine receptor type 3
CD40L	CD40 ligand
cDNA	Complementary deoxyribonucleic acid
C/EBPalpha	CCAAT/enhancer binding protein, alpha
cMyc	myelocytomatosis viral oncogene homolog (avian)
COL3A1	Collagen type 3A1
COLEC12	Collectin subfamily member 12

COX-2	Cyclooxygenase 2
CREB1	cAMP responsive element binding protein 1
CSH	Chorionic somatomammotropin hormone
CTLA4	Cytotoxic T – lymphocyte associated antigen – 4
D-PBS	Dulbecco's phosphate buffered saline
DTT	Dithiothreitol
DMRT1	Doublesex and mab-3 related transcription factor 1
dNTP	Deoxyribonucleotide triphosphate
EGR	Early growth response
ELN	Elastin
ER	Endoplasmic recticulum
ESR	Estrogen receptor
Ets-	E-twenty six
FAM	6-carboxyfluorescin
FCGRT	Fc fragment of IgG, receptor, transporter, alpha
FGF	Fibroblast growth factor
FOLH1	Folate hydrolase
FOS	FBJ murine osteosarcoma viral oncogene homolog
FOXM1	Forkhead box M1

FSMM	First strand master mix
GCOS	GeneChip operating software
GHR	Growth hormone receptor
GMCSF	Granulocyte macrophage colony stimulating factor
GO	Gene ontology
HG -U133	Human Genome U133 Plus 2.0
HP	Haptoglobin
HSF	Heat shock transcription factor
IGF-1	Insulin growth factor -1
IL-	Interleukin –
ILT	Intraluminal thrombus
IRE-1	Endoplasmic recticulum to nucleus signalling-1
IVT	In-vitro transcription
KIR2DL1	killer cell immunoglobulin-like receptor, two domains, long cytoplasmic tail, 1
MAC	Membrane attack complex
MMP	Matrix metalloproteinase
MSX1	Msh homeobox 1
MTHFD1	Metylenetetrahydrofolate dehydrogenase 1
MTHFR	Methylenetetrahydrofolate reductase

MTR	5 methyltetrahydrofolate homocysteine methyltransferase
MYOG	myogenin (myogenic factor 4)
NA	Normal Aorta
NF	Nuclear factor
NFAT	Nuclear factor of activated T cells
NK	Natural Killer cells
NNMT	nicotinamide-N-methyltransferase
NSAID	Non steroidal anti-inflammatory drug
NT-3	3' nucleotidase
ODN	Oligodeoxynucleotide
OPN	Osteopontin
PA	Plasminogen activator
PAI	Plasminogen activator inhibitor
PAX	Paired box
PCA	Principle component analysis
PDGF	Platelet derived growth factor
PGE-2	Prostaglandin E 2
PON-1	Paraoxonase 1
PPARγ	Peroxisome proliferator-activated receptor gamma

PTFE	Polytetrafluoroethylene
qRT- PCR	quantitative Real Time Polymerase Chain Reaction
RAR	Retinoic acid recptor
RANKL	Receptor activator of NF-kappa-B ligand
RCT	Randomised control trial
RNA	Ribonucleic acid
ROS	Reactive oxygen species
SD	Standard deviation
SDF-1	Stromal cell derived factor-1
SHP	Small heterodimer partner
SMC	Smooth muscle cell
SMM	Second strand mastermix
SNPs	Single nucleotide polymorphisms
SP	Specificity protein
SRB-1	Scavenger receptor class B member 1
SREBP	Sucrose responsive element binding protein
SRF	Serum response factor
STAT	Signal transducer and activator of transcription
TAMRA	Tetramethylrhodamine

TCR	T cell receptor
TGF-	Tumour growth factor
Th1/Th2	T helper
TIMP	Tissue inhibitor of matrix metalloproteinase
tPA	Tissue plasminogen activator
TYMS	Thymidylate synthetase
UKHTB	United Kingdom Human Tissue Bank
uPA	Urokinase-type plasminogen activator
VEGF	Vascular endothelial growth factor
VSMC	Vascular smooth muscle cell
WT-1	Wilm's tumour – 1

List of Figures

List of Tables

ABSTRACT

Introduction

Abdominal aortic aneurysm (AAA) is a common disorder and a major cause of death. Pathological processes involved in AAA formation include inflammation, proteolysis, angiogenesis and apoptosis. It has also a strong familial predisposition with linkage studies identifying chromosomes 19q13 and 4q31 as susceptible loci. AAA is likely to be a polygenic disorder.

Aims

The aims of this study were to carry out a whole transcriptome analysis in order to identify novel genes and pathways that are differentially expressed between aneurysmal (AAA), atheromatous (AOD) and normal (NA) aortic tissue and to confirm a set of these differentially expressed genes using quantitative real time polymerase chain reaction (qRT-PCR).

Methods

RNA samples were prepared from full thickness aortic walls obtained during open repair of AAA, aortic bypass for AOD and transplant patients for NA. The quality of the RNA was assessed using the Bioanalyzer 2100 (Agilent) and Nanodrop. RNA was then reverse transcribed to cDNA which was then hybridised to the Human Genome (HG) -U133 plus 2.0 microarray (Affymetrix) that interrogates the whole human genome. The robustness of the genearray was assessed using data output quality control as defined by Affymetrix. Statistical analysis was then carried out using the GeneSpring software. Genes

were considered to be significantly differentiated if they had at least a two-fold change and a P-value < 0.05 following Benjamini-Hochberg multiple correction testing. Genes were then classified according to their molecular functions. A set of consistently differentially expressed genes were confirmed using qRT-PCR with Taqman probes on a larger sample size compared with the microarray experiment. All pathway and network analysis on the differentially expressed genes were conducted using MetaCore software Version 6.3 (GeneGo, Inc).

Results

A total of 3320 genes and 233 genes were differentially expressed when comparing AAA with NA and AAA with AOD respectively. There was a predominance of inflammatory and proteolytic genes in AAA wall. Genes with differential expression were identified on chromosome 19q13, a locus that has been genetically linked with AAA. These included CD79A and SpiB transcription factor which were upregulated in AAA. Both genes are involved in inflammatory pathways. Of the nine genes confirmed on qRT-PCR, eight showed similar trends to that in the microarray experiment. On pathway analysis, immune and inflammatory themes predominate.

Conclusions

This study reveals the differential expression of 233 genes in AAA compared with AOD. This includes a number of novel genes that have not been previously linked to AAA, some of which lie on chromosome 19q13, a locus that has been genetically linked with AAA. The analysis also confirms a number of genes that are already reported to be differentially expressed in AAA compared with NA or

AOD. Currently, there is no diagnostic test that can predict the growth rate of AAA and no drug to modulate its growth. The novel genes and pathways identified in this study may be putative biomarkers or therapeutic targets for AAA.

Chapter 1

OVERVIEW of AAA

1.1 Definition

The word aneurysm is derived from the Greek word ‘aneurusma’ meaning widening. In the Oxford Dictionary it is defined as ‘an excessive localized swelling of the wall of an artery’. However in clinical practice, it is important to define exact measurements to determine what constitutes ‘swelling’ and ‘dilatation’ so that diagnostic and therapeutic targets can be set.

The diameter of the infrarenal aorta has been studied in necropsy and ultrasound screening. The average diameter is 2.10 cm[1] and is known to enlarge with age, race, sex and body surface area but these effects are small though statistically significant[2-4].

McGregor et al proposed a definition of an abdominal aortic aneurysm as an aorta with an infrarenal diameter of greater than 30mm[5]. In 1991, the Society for Vascular Surgery and the International Society for Cardiovascular Surgery Ad Hoc Committee on Standards in Reporting proposed as a criterion that the infrarenal diameter should be 1.5 times the expected normal diameter[6]. The disorder is conventionally diagnosed if the aortic diameter is 30mm or more.

1.2 Epidemiology

The prevalence of AAA can be inferred from necropsy and population-based screening programmes. Studies with high necropsy rates showed a prevalence of 0.6% to 3.2%[7-12]. In table 1.1, a survey of the necropsy studies is presented. There has been a tendency for AAA to increase in frequency over time. The age- and sex-specific frequencies of AAA were only calculated in two of the listed necropsy studies[7;8]. In both studies, the total aneurysm frequency was twice as high in men as in women and the aneurysms tend to appear later in woman.

Table 1.1 Necropsy-based studies of abdominal aortic aneurysm[13]

***Assuming 50% of autopsies to be in males**

Author	Period	Autopsies (n)	Frequency	M/F ratio	Increasing trend
Burch & DePasquale[8]	1947 – 1957	26 554	0.6	3.5*	-
Darling et al.[14]	1952-1975	24 000	2.0	2.6*	-
Kunz[10]	1954-1978	35 380	1.7	2.2	-
Rantakokko et al.[11]	1959 – 1979	22 765	0.8	-	Yes
Sterpetti et al[12]	1956-1986	44 144	0.6	4.0*	Yes
Bengtsson et al[13]	1958-1986	45 838	3.2	2.0	Yes

Ultrasound scanning is a cheap, acceptable and non-invasive method of screening for AAA. It has an estimated sensitivity and specificity of 98 and 99%[15], respectively. Four large randomised control trials[16-19] have so far been carried out. Of the 125,183 men over 65 years old that were screened, the overall prevalence rate was 5.5%.

Table 1.2 Characteristics of the four randomised screening trials for abdominal aortic aneurysms[20]

	Vyborg study[18]	Western Australia[19]	MASS[16]	Chichester[17]
Age	64–73	65-83	65-74	65-80
No. Participants	12 639	38 704	67 800	6040
Follow-up (years)	9.6	3.6	7	15
Attenders (%)	77	63	80	73
AAA prevalence	4.0%	7.2%	4.9%	7.7%

1.3 Population screening

Population screening for AAA has only relatively recently started in the UK. It has been estimated that a single ultrasound scan in males over the age of 65 years would detect 90% of aneurysms at risk of rupture[21]. The MASS trial has provided good evidence that the prevalence of aneurysm-related death is significantly reduced in a screened male population aged 65-74 years, with a 53% reduction

in those who attended for screening[16]. The MASS trial data also showed that over four years the mean incremental cost-effectiveness ratio for screening was £28400 per life year gained, equivalent to approximately £36000 per quality adjusted life-year. It was estimated that this would fall to approximately £8,000 per life year gained at 10 years[22]. The case for population-based screening for AAA is therefore convincing.

1.4 Clinical presentation

Most AAAs are asymptomatic. They are found on routine medical examination when a central abdominal pulsatile mass is discovered during abdominal palpation. They cause severe abdominal pain and hypovolaemic shock when they rupture. Many patients develop symptoms of chronic back pain as a result of pressure on the lumbar vertebrae, which may be eroded. Thrombosis, distal embolisation and rupture into the intestine or vena cava are rare complications[23].

1.5 Risk Factors

The aetiology of AAA is multi-factorial. Positive associations with AAA include age[24-26], smoking, hypertension and chronic obstructive airway disease[25-30] whereas diabetes and black race are negatively associated[28]. Genetics also plays an important part in the pathogenesis of AAA. Since Clifton[31] in 1977 described AAA in three elderly male siblings in the absence of an associated connective tissue disorder, other series have confirmed familial clustering with

aneurysms found in 11-20% of first degree relatives[32-39]. The risk is more pronounced in males than in females (25% vs. 7%)[35]. There is approximately a 7-fold increase in the prevalence of AAA in male siblings of affected individuals compared with controls and an 18-fold increase of AAA in male siblings of affected individuals aged over 60 years[40;41]. Patients with a family history tend to present younger and have a greater rate of rupture providing further evidence of a genetic component[42]. Familial predisposition is therefore a strong risk factor in the development of AAA.

A monogenic disorder resulting in AAA has not been found. There are however monogenic diseases that have been associated with aortic aneurysms and dissections (TAAD) including Marfan's syndrome[43], Ehler's Danlos type IV, autosomal dominant cutis laxa (caused by mutations in the elastin gene[44]) and autosomal recessive cutis laxa (caused by fibulin-4 gene mutations[45]).

1.6 Management of AAA

1.6.1 Historical

In 1555, Vesalius was the first to diagnose an AAA. Astley Cooper was first to ligate the abdominal aorta for a ruptured iliac aneurysm in 1817. In 1923, Matas performed the first successful aortic ligation in a patient with AAA and introduced the concept of endoaneurysmorrhaphy. Others attempted to induce thrombosis of AAA by inserting intraluminal wires. In 1948, Rea wrapped reactive cellophane

around the neck and the anterolateral surfaces of an aneurysm to induce a fibrotic reaction and thereby limit expansion. Nissen used this technique in 1949 to treat the symptomatic AAA of Albert Einstein, who survived 6 years before succumbing to rupture. The first successful and durable management of AAA was described by Charles Dubost in 1951[46].

1.6.2 Surgical management

Surgery is the mainstay of treatment for AAA. Two forms of repair are currently available for the elective management of AAA. Standard open surgical repair has been in widespread use for the last 50 years. Recently endovascular repair of AAA has been increasingly used as it is less invasive. Most AAA never rupture[14], so deciding when to electively repair an AAA and by what method, can be difficult.

i) Repair vs. Surveillance for small AAA.

Necropsy[9] and clinical studies[9;47] have shown that the risk of rupture of AAA increases with aortic diameter. It has been recommended that aneurysm > 5.5 cm should be electively repaired. The management of small aneurysms i.e. 4.0-5.5 cm has been addressed in two randomised control trials: UKSAT[48] and ADAM[14;49]. Both trials compared all-cause mortality after immediate elective open repair of AAA with a policy of imaging surveillance with repair of AAAs that enlarged greater than 5.5 cm or become symptomatic. Early surgery did not

provide a long-term advantage in both trials and ultrasonographic surveillance was recommended for AAA ranging from 4.0 to 5.5 cm.

ii) Open repair vs. Endovascular repair.

Four trials[50-53] have reported outcomes of open repair versus endovascular repair of large AAAs in patients who were candidates for both procedures. They have shown reduced operative mortality and early improvement in quality of life with endovascular repair but did not find a difference in mid-term all-cause mortality or quality of life. Endovascular repair is associated with more re-interventions and requires periodic imaging for the remainder of the patients' life. Longer term follow-ups are required to determine the relative effects of the two procedures on all-cause mortality.

iii) Endovascular repair versus observation in patients who are unfit for open repair

EVAR-2[54] was the only randomized trial to compare endovascular repair with observation for patients who are unfit for open repair. There was no survival benefit from endovascular repair despite its minimally invasive approach.

iv) Endovascular repair versus surveillance in patients with small abdominal aortic aneurysms

Endovascular repair of AAA is associated with a lower mortality than open surgical repair[50]. Further, retrospective reviews of EVAR databases have shown

that endovascular repair of small AAAs are associated with a better outcome than large AAAs. About 1.9–3.2%[48;49] of small AAAs will rupture while on surveillance. The PIVOTAL trial is a multicentre randomised study comparing outcomes between endovascular repair of small AAAs (4.0-5.0 cm) and surveillance[55].

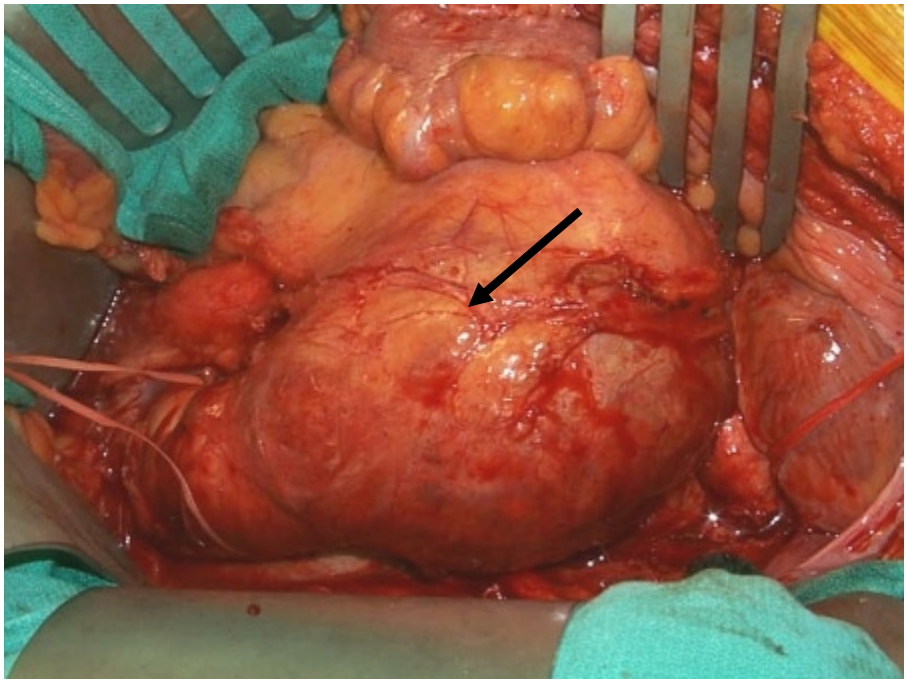


Figure 1.1 Open repair of AAA (black arrow).

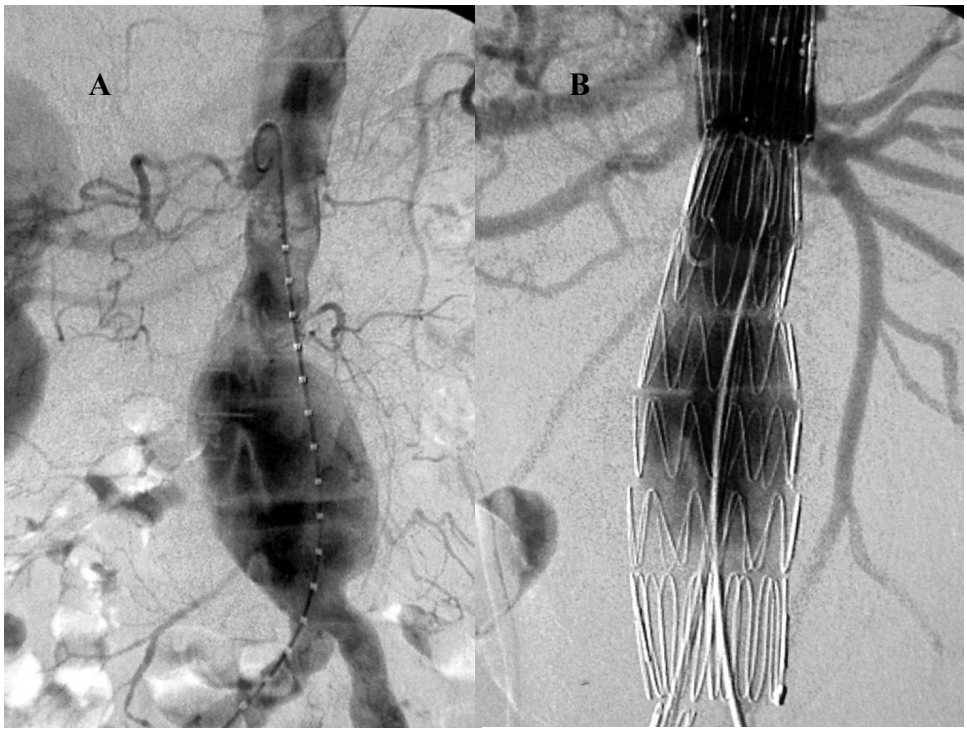


Figure 1.2 Angiogram showing endovascular repair of AAA. A) AAA prior to stent deployment B) AAA after stent insertion

1.6.3 Medical management of AAA

Medical treatment of AAA is still at an experimental stage. Current medical treatments used in human trials are discussed below.

i) Beta-blockers

Beta-blockers have been shown to improve cardiac morbidity and mortality following major vascular surgery in high risk cardiac patients[56]. Its haemodynamic effect on systolic blood pressure is also potentially beneficial in controlling AAA expansion. Propanolol has also been shown to be beneficial in animal models of aneurysmal disease based on its biochemical effects on matrix proteins[57;58]. Propanolol was investigated in two large multicentre randomised control trials[15;59] for AAA. However, it was poorly tolerated in both trials and there was no reduction in AAA growth rate. Propanolol also had a significant negative effect on quality of life[59] as would be expected from the poor compliance rates in both studies.

ii) MMP inhibitors

Tetracyclines are non-specific MMP inhibitors whose mechanism of action is similar to endogenous tissue inhibitor of metalloproteinases (TIMPs) and is unrelated to their anti-microbial action[60;60;61]. Tetracyclines have also been shown to have a profound but selective effect on vascular inflammation and reduce aortic wall neutrophil derived proteases and cytotoxic T-cell content[62].

The use of doxycycline in reducing AAA expansion in man has so far had mixed results. A small randomised control trial (RCT) involving 32 patients suggested that there may be a positive effect of treatment on AAA size over an 18-month period[61], while a prospective multicentre study showed no significant change in AAA expansion over 6 months[33]. Compliance was high in both trials. Tetracycline's efficacy in reduction of AAA growth needs to be proven in a large RCT over a longer period (given the non-linear nature of aneurysm expansion) before it can be recommended as a therapeutic agent.

iii) Angiotensin Converting Enzyme (ACE) inhibitors

ACE inhibitors reduce formation of angiotensin II and are therefore potent antihypertensive. They have therefore been investigated as a potential therapeutic agent in slowing AAA expansion as high blood pressure is associated with AAA development. ACE inhibitors have also been shown to upregulate collagen synthesis and decrease aortic stiffness[63;64]. However, post-hoc analysis of the UK aneurysm trial data showed no relationship between the use of ACE inhibitors and decreased expansion rate of small AAA[64]. A retrospective study analysing ruptured and non-ruptured aortic aneurysms over a 10-year period showed that use of ACE inhibitors may protect against rupture[65]. Their effect on collagen synthesis could explain the decreased risk of ruptured AAA in patients receiving them. The AARDVARK trial (funded by the National Institute for Health Research, UK) is currently investigating the potential aneurysm-related benefits

of perindopril, an ACE inhibitor, in patients found to have small AAAs at screening.

iv) Statins

Statins exhibit both anti-inflammatory and anti-proteolytic properties both of which play important roles in the pathophysiology of AAA. Their use has been associated with decreased levels of MMP-3, MMP-9[66] and cysteine proteases[67] in explant biopsies of AAA. AAA expansion is inhibited and even reduced[68] in patients receiving statins. Mortality was also decreased[68]. All patients with abdominal aortic aneurysms are considered to be at risk of a major cardiovascular event and should be started on a statin[69]. The elucidation of the exact mechanism of action of the statin could lead to the development of specific inhibitors of AAA growth.

v) Anti-inflammatory agents

Anti-inflammatory agents are thought to decrease AAA expansion through inhibition of COX-2. This decreases the amount of PGE2, which in turn inhibits the production of MMPs[70]. Non-steroidal anti-inflammatory drugs have been shown to decrease AAA expansion from 3.2 to 1.5mm/year[71]. COX-2 inhibitors are, however, unlikely to be investigated further as potential therapeutic agents because of their association with thrombotic events, notably myocardial infarctions[72-74]. The use of steroids and cyclosporine for long-term control of AAA expansion is unpractical because of their immunosuppressant effects.

vi) Other drugs

Rapamycin is a macrolide antibiotic with an immunosuppressant effect that has been shown to be effective in reducing aneurysm growth in an elastase-induced model of AAA in rats[75]. Human trials are awaited. Roxithromycin, an antibiotic with bactericidal action against Chlamydia has been shown to be effective in reducing the expansion rate of AAA in a RCT, but this effect was only sustained for a year[76]. Disodium cromoglycate, an inhibitor of mast cell degranulation, reduced aortic expansion by 40% in an elastase-induced mouse AAA model, accompanied by the inhibition of recruitment of mast cells and macrophages[77]. Similarly, treatment with tranilast, another mast cell degranulation inhibitor, attenuated AAA progression in a $CaCl_2$-induced rat AAA model[78]. Rosiglitazone, a peroxisome proliferator activated receptor gamma agonist (PPARγ), reduced aortic expansion and rupture in angiotensin-II induced hypercholesterolemic mouse model. Decrease in aortic expansion is associated with decreased expression of inflammatory mediators[79]. Rosiglitazone is unlikely to be used in human trials for AAA due to its cardiovascular side-effects. However, pioglitazone another PPARγ agonist is a potential therapeutic target due to its more favourable side-effect profile[80].

vii) Gene Therapy

Gene therapy is still at an experimental stage in the prevention of AAA development. Elastase-induced AAA development in rats was successfully inhibited using chimeric decoy oligodeoxynucleotides (ODN) against NF-κB and

Ets with a reduction of MMP expression[81]. Adenoviral transfection of TGF-β1 promotes the stability of expanding AAA[82]. Endovascular seeding of syngeneic vascular smooth muscle cells (VSMCs) in aneurysmal aortic xenografts in rats restores the healing capabilities of proteolytically injured extracellular matrix in aneurysmal aortas, and stops expansion[83] . These results are encouraging in that possible drug targets have been identified. There are, however, limitations to gene therapy for AAA. It is short-lived (transgene expression of TGF-β1 is exhausted by 28 days)[82] so that multiple rounds of gene therapy may be required for the treatment of AAA and it has the potential to elicit an adverse immune response. In addition, there is always the fear that any viral vector, once inside the patient, may recover its ability to cause disease. It may also be naïve to think that sporadic AAA is treatable using single gene therapy, as it is a polygenic disorder. The development of novel less immunogenic vectors, capable of carrying multiple genes, would be required for gene therapy to be considered a viable option for the treatment of AAA.

1.7 PATHOGENESIS OF AAA

1.7.1 Structure of the abdominal aortic wall

The abdominal aorta has three distinct histological layers: intima, media and adventitia. The luminal side of the tunica intima is lined by a layer of endothelial cells. The tunica media has a lamellar structure consisting of smooth muscle cells, elastin, collagen and ground substance. The tunica adventitia is composed

of loose connective tissue with fibroblasts and associated collagen fibres, as well as nutrient microvessels (the vasa vasora).

Elastin and collagen form the major components of the extracellular matrix. Elastin is laid down in a lamellar structure within the media and constitutes about 30% of the dry weight of the aorta[84]. Most of the elastin in arteries is present as the insoluble tropoelastin monomers that are cross-linked by lysine residues. It is produced during early development and its production is complete by maturity. Elastin then remains fairly stable with an estimated half-life of 40 to 70 years[85]. It provides support in both circumferential and longitudinal directions and distributes tensile strengths uniformly along the aortic wall[85;86]. It also provides elastic recoil to the dilated aortic wall.

Collagen is present mainly as triple helical type I and type III fibrillar collagen in a ratio of 2:1 in the aortic wall. They are the main components of the outer layer of the adventitia[87], where they provide tensile strength and stiffness to the arterial wall[87]. Unlike elastin that can stretch up to 70%[88] of its initial length, collagen can only stretch up to 2-4% of its uncoiled form[88].

1.7.2 Extracellular matrix turnover

Histological examination of AAA wall has shown that it is mainly a disease of the media and to a lesser extent the adventitia. It is characterised by a decrease in the thickness of the media, disruption of the medial connective tissue structure

and the loss of elastin[87]. This disturbs the integrity of the lamellar structure of the media that is important in preventing aneurysm formation[87]. Elastolysis and lamellar disruption are the goals of the elastase infusion used to induce aortic dilatation in animal models[89]. Aneurysm formation is not only characterised by a change in the ratio of the constituents of the extracellular matrix (with an increase in collagen and a decrease in elastin)[90], but also by the presence of immature, un-linked forms of both collagen and elastin[90].

These changes in the media have been the focus of much AAA research in an attempt to unravel the pathogenesis of this disease. Biomechanical studies of arteries subjected to endarterectomy have, however, demonstrated that the aortic adventitia could tolerate both longitudinal and radial stress energy[91] and suggesting that the integrity of the aortic wall might also rely on the collagen rich outer media and adventitia.

1.7.3 Inflammation and auto-immune response

Inflammation plays an important role in the pathophysiology of AAA development. The walls of aortic aneurysms contain large number of inflammatory cells including lymphocytes, macrophages and plasma cells[92] as well as deposition of immunoglobulin G. Further in-vivo evidence of AAA as an inflammatory disease is the presence of inflammatory cells in the aortic wall of elastase-infusion model of AAA at day 7 when aortic dilatation is maximal

compared with day 1 when there is minimal dilatation and no inflammatory response[93].

Autoimmunity involves the breakdown of self immunoregulatory processes and tolerance leading to generation of an immune response against self-antigens. Another mechanism is 'molecular mimicry' whereby common antigenic epitopes are shared between a microorganism and a self-antigen. A response against the microorganism may lead to a similar response against the self-antigen sharing common epitopes with the microorganism. Molecular mimicry is responsible for several autoimmune diseases[94]. There is sufficient evidence to suggest that AAA is an antigen-driven autoimmune disease as discussed below.

Global gene expression profiles of AAA tissue reveal large number of genes related to the immune system. Microarray based gene expression studies of AAA wall compared with NA show that there are a number of differentially expressed genes involved in immune responses[95;96]. This further highlights the role of inflammatory pathways in the pathogenesis of AAA.

Immunohistochemical examination of AAA wall has shown extensive mononuclear cell infiltrates in the adventitia and to a lesser extent the media of AAA[97-101]. A predominance of CD3+ve T - cells was noted in the adventitia of AAA compared with AOD and NA. CD19+ve B - cells and CD11c +ve macrophages were present in the adventitia of all pathological tissues[100]. In

another study characterising vascular associated lymphoid tissue in AAA wall, the predominance of T-cells was also noted, although over 50% of samples showed typical lymphoid follicles with B-cell germinal centres[100]. AOD is however a disease of the intima rather than the adventitia. Atherosclerotic plaques of AAA wall were also found to have a significant proportion of CD4 T-cells, NK cells and NK T-cells[97].

1.7.3.1 TH1 TH2 responses The immune response is either cell-mediated (Th1 response) or humorally-mediated (Th2 response). Inflammatory cells found in the walls of aortic aneurysms release cytokines that modulate the cellular and humoral immune response. Th1 cytokines such as IFN-γ, IL-2, IL-12, IL-15 and IL-18 are elevated in the blood and aortic tissues of patients with AAA[102]. Serum-IFN-γ correlates with the rate of aneurysm progression[103]. Th2 cytokines such as IL-4, 5, 8 and 10 regulate the immune response and smooth muscle cell apoptosis[102-104].The latter is a feature of aneurysm development.

Aneurysm development involves a complex interaction between Th1 and Th2 immune responses[105]. Th1 cytokines potentiate early atherosclerotic development[106] while Th2 cytokines are present in the AAA wall in late stages of human AAA disease[105]. A Th1 response promotes aneurysm formation by inducing the expression of matrix-degrading proteinases, while a Th2 response suppresses macrophage MMP production and limits aneurysm formation[107]. IL-4 antagonism (i.e. antagonism of a Th2 response) attenuates the formation of

aortic aneurysm in a murine aortic transplantation model[105]. Schimizu at al explain their conflicting results with other studies by postulating that a Th1 response is essential for recruitment of inflammatory cells and atheroma formation, but without a Th2 response the lesion progresses towards aortic occlusive disease[105]. Triggering of a Th2 response leads to extracellular matrix degradation and aneurysm formation. Such triggers include risk factors for AAA such as smoking and aging[105].

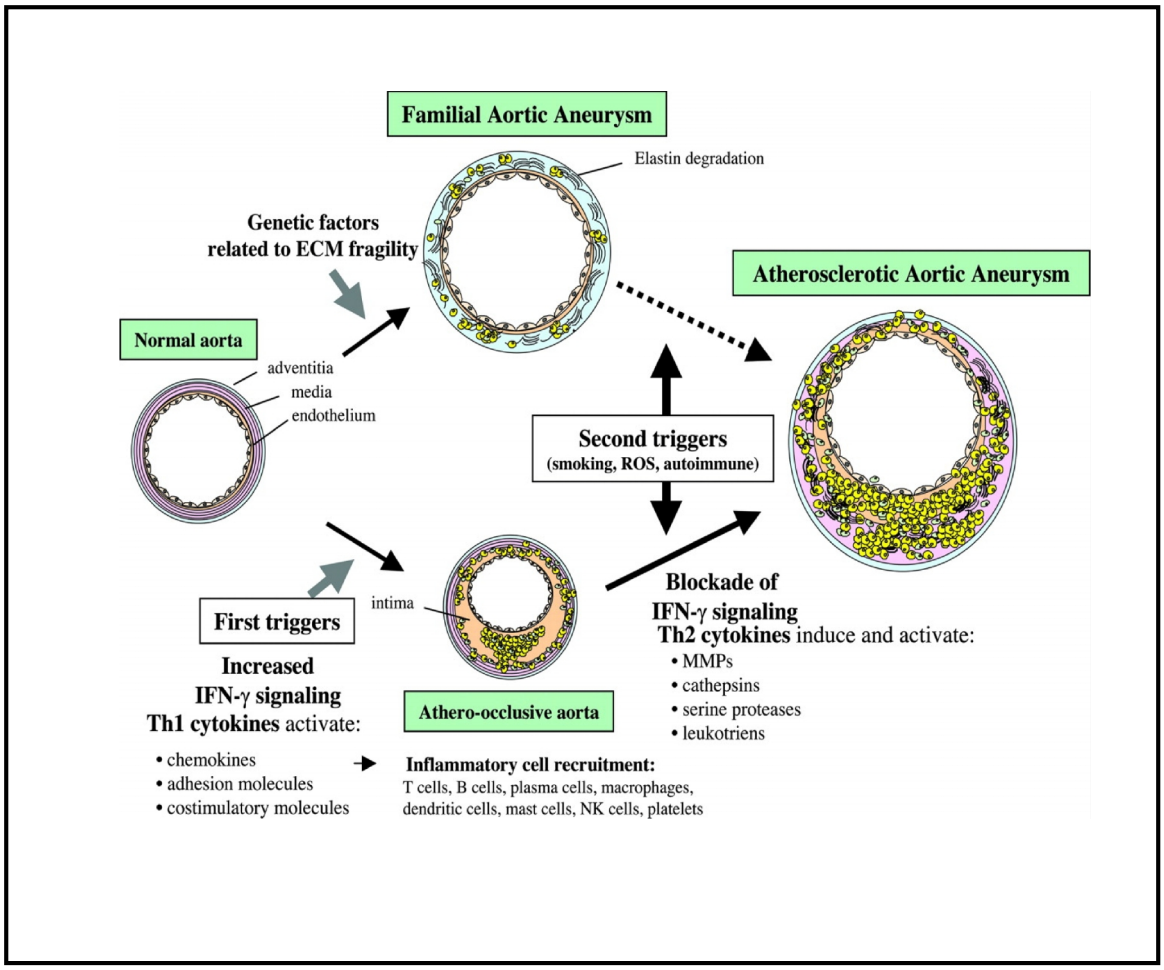


Figure 1.3 Hypothetical scheme of Th1/Th2 response in aneurysm development. [105]

1.7.3.2 Antigen activation in wall of AAA Mononuclear cells infiltrating AAAs express early activation (CD69), intermediate activation (CD25, CD38) and late activation (CD45) antigens. The expression of these antigens suggests active ongoing inflammation in these lesions[108].

1.7.3.3 Autoantibodies and AAA B cells and plasma cells are localised in the walls of AAAs and express CD69 and CD80 activation markers[109]. Levels of IgA and IgG positive B-cells are higher in AAA lesions compared with the same cells found in the peripheral blood of the same patient[109]. Walton et al showed increased concentration of B-cell infiltrate in the adventitia of AAA wall. However, they failed to show a restricted usage of immunoglobulin genes from the DNA isolated from the aneurysmal wall. This indicates that the B-cell adventitial infiltrate is not an autoimmune response to a limited repertoire of tissue antigens[110].

Immunosuppressive drugs such as rapamycin[75], methyl prednisolone, and cyclosporine[111] reduce the rate of growth of AAA in animal models. This further supports the possibility that AAA is an autoimmune disease.

1.7.3.4 Putative self and non-self antigens involved in cellular and antibody responses in AAA Several possible self and non-self antigens have been identified in AAA wall that may be involved in the pathogenesis of aneurysm development (summarised in Table 1.3). These antigens may be able to initiate AAA by molecular mimicry as described above.

Chlamydia pneumoniae is among the most widely studied non-self antigen. Its presence in the walls of AAA has been shown by immunohistochemical analysis

and tissue culture. However, polymerase chain reactions have failed to show the presence of Chlamydia pneumoniae DNA[112].

Table 1.3 Putative antigens that may elicit cellular and humoral responses in AAA[113]

Self antigens	Non-self antigens
Elastin and Elastin fragments[108]	Chlamydia Pneumoniae[108]
Collagen type I[108]	Cytomegalovirus[108]
Collagen type III[108]	Salmonella[108]
AAAP-40[114;115]	Treponema palladium[108]
Oxidised low-density lipoprotein[108]	

1.8 Proteolysis and extra-cellular matrix remodelling

Abdominal aortic aneurysm formation is characterised by a breakdown of the extracellular matrix in the aortic wall, which consists mainly of elastin and collagen. Elastinolysis is pertinent to vessel dilatation, whilst collagenolysis plays an important role in aneurysmal rupture[85].

1.8.1 Matrix metalloproteinases

MMPs are a family of zinc- and calcium-dependent proteases with proteolytic activity against components of the extra-cellular matrix. There are 25 known MMPs out of which 23 are present in humans[116].

All MMPs have a similar structure consisting of a protease domain and an ancillary domain connected by a flexible proline-rich hinge peptide except for MMP-7 (matrilysin-1) and MMP-26 (matrilsin-2). These MMPs lack the ancillary domain. The protease domain contains a signal peptide, a pro-domain and the catalytic module. The ancillary domain is most commonly a domain similar to sequences in the heme-binding protein hemopexin and the soluble fibronectin-related protein vitronectin[117;118]

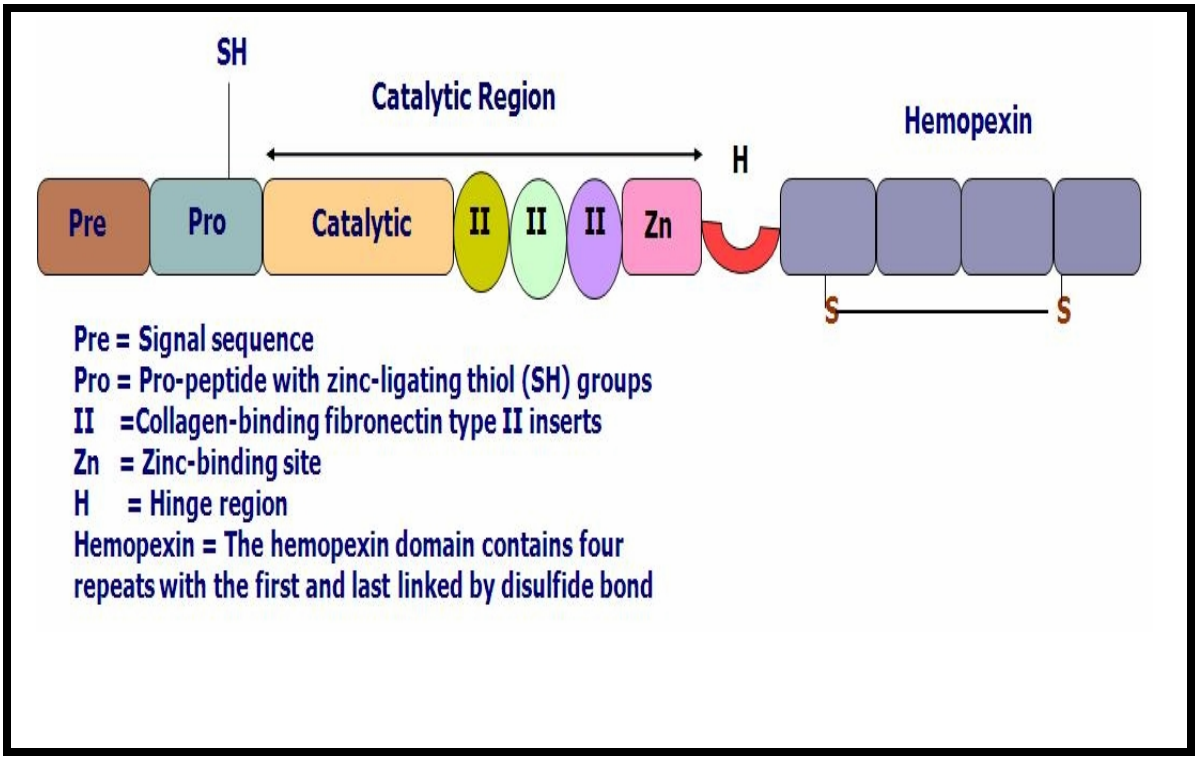


Figure 1.4 Basic domain structure of the matrix metallopeptidases.[118]

Due to their high proteolytic activity, MMPs are strictly regulated at three levels: intra-cellular transcription, extra-cellular pro-enzyme activation and inhibition by endogenous tissue inhibitors of MMPs (TIMPs)[119]. The major activator of MMPs is plasmin, which is the product of the action of plasminogen activators on plasminogen[120]. The elastin specific MMPs and their inhibitors: MMP-2, MMP- 3, MMP-8, MMP-9, MMP-12 and TIMPs are of particular interest in AAA pathophysiology[120].

MMP-2 and -9 are the most extensively studied MMPs in patients with AAA. MMP-2 levels in the AAA wall correlate positively with increasing AAA

diameter[121]. MMP-9 is suggested to be responsible for continued expansion and rupture of aneurysms and is less prevalent in smaller aneurysms[121;122]. Its primary source is inflammatory cells infiltrating the arterial adventitia, and it has been immunolocalised to both macrophages and B cells[121]. Unlike either MMP-2 or -9, MMP-3 mRNA is upregulated by more than 80-fold in AAA wall compared with levels in AOD wall[123].

MMP-8, a potent type I collagenase, was found to be elevated at the protein level in ruptured AAA wall compared to unruptured AAA wall[122]. Similar result was not reproducible at the transcription level[123] reflecting the fact that MMP-8 may be stored as preformed protein granules and thus mRNA levels may not be representative of protein concentration.

MMP-12 is produced by macrophage and degrades collagen, elastin and laminin[124]. MMP-12 has been identified in the wall of AAA but not in AOD or NA walls[124]. Extracted MMP-12 from AAA wall also showed in-vitro activity[125]. MMP-13 is localised to VSMCs and degrades collagen[126]. It has been associated with AAA rupture[126].

TIMPs constitute a family of four glycoproteins (TIMP-1,-2,-3 and -4) that inhibit MMP and ADAM activity by binding to the catalytic sites of these enzymes[127]. Among these four TIMPs, only TIMP-1 has been shown to have a protective

effect against AAA development by inhibiting both MMP-1 and MMP-9[127]. These have been confirmed in animal models of AAA[128;129].

Table 1.4 MMPs and TIMP associated with the pathogenesis of AAA[130]

Mediators	Cells of origin	Role in AAA
MMP-1	Fibroblasts	Collagenase: AAA rupture
MMP-2	VSMC fibroblasts	Elastin degradation
MMP-3	Macrophages	Elastin and collagen degradation
MMP-8	Neutrophils	Collagenase: AAA rupture
MMP-9	Macrophages / Neutrophils	Elastin degradation Collagenase: AAA rupture
MMP-12	Macrophages	Elastin degradation
MMP-13	VSMCs	Collagenase: AAA rupture
MMP-14	Macrophages / VSMCs	Activates proMMP-2
TIMP - 1	Various cell lines	Protective role by inhibiting MMP -1, -9 and ADAM-10

1.8.2 Cysteine proteases

Cathepsins are a large family of lysosomal cysteine proteases that play a vital role in mammalian cellular turnover. They have potent collagenase and elastase activities[131]. Cathepsin S is one of the most potent elastase known[131], while

Cathepsin K cleaves the triple helix of collagens I and III[132]. Both enzymes are localised within smooth muscle cells and macrophages within atherosclerotic plaques[132]. Cathepsins D, H and L are involved in the degradation of structural proteins and there is greater activity in AAA wall and mural thrombus than in normal aortic wall[133-135]. Deficiency of cystatin C, an inhibitor of cysteine protease, is associated with increased aneurysm size and expansion rate[136].

1.8.3 Serine Proteases

Cleavage of the plasma protein, plasminogen, by plasminogen activators generates plasmin, which is the classical fibrinolytic enzyme (Figure 1.5). This reaction is controlled by the plasminogen activator inhibitor (PAI-1). Plasmin activates MMPs[137] and in this way may have an indirect role in extracellular matrix degradation during AAA development[86;134;138]. AAA wall contains significant levels of both plasminogen activators (tPA and uPA)[134]. Expression of PAI-1 at the transcriptional level in AAA wall has also been shown to be significantly lower compared with AOD wall[139]. Plasma levels of plasmin-antiplasmin complexes correlate positively with progression of small AAA to large AAA requiring surgical intervention[140].

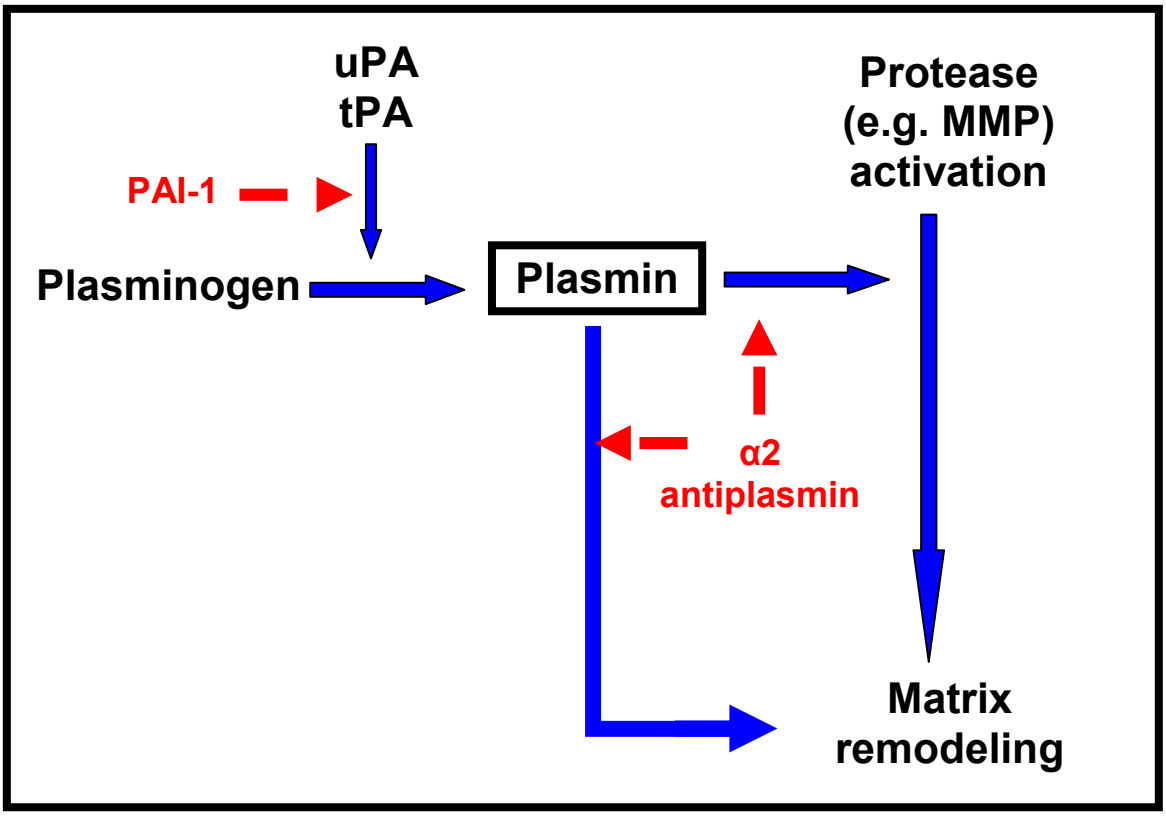


Figure 1.5 The plasminogen-plasmin system. Plasminogen is converted into its active form plasmin by uPA and tPA. Plasmin promotes matrix degradation through activation of MMP and growth factors. Plasminogen activator inhibitor-1 (PAI-1) is the physiological inhibitor of PAs.

1.9 Angiogenesis

Healthy infrarenal aortic media unlike the thoracic aorta is devoid of vasa vasorum[141]. Medial neovascularisation is, however, a consistent histopathological feature of AAA wall (Figure 1.6) and has been spatially correlated with destruction of elastin and chronic inflammation[142].

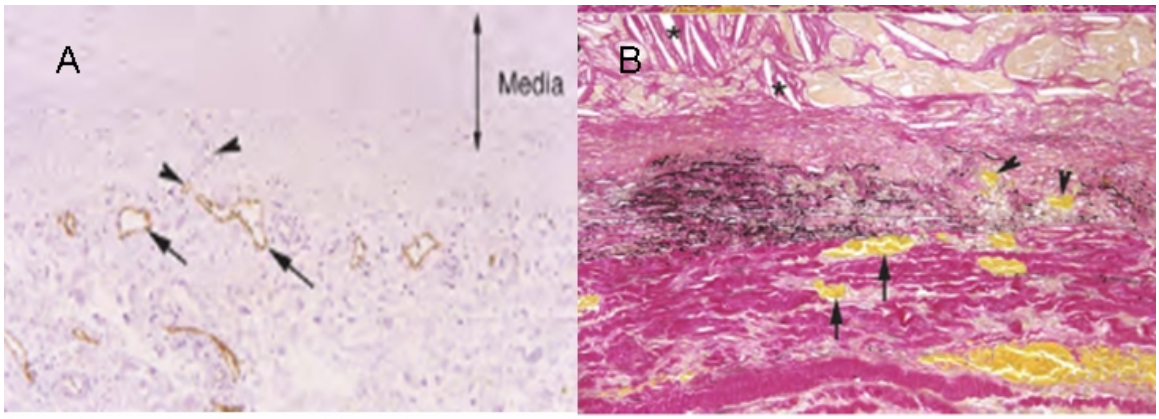


Figure 1.6 A) Normal aorta – extensive network of vasa vasorum in adventitia (arrows) with some vessels extending into media. B) AAA – neovascularization of the media (arrowheads) originating from adventitial vasa vasorum (arrows)[143].

It has therefore been proposed that these new vessels have a sustaining or even a causal role in the pathophysiology of aneurysms by secreting proteases that destabilise the extracellular matrix[144] and also possibly acting as a conduit for more inflammatory cells. Immunohistochemical studies confirm localisation of

proteinases such as MMP-2 and MMP-1[144] in the neovascular endothelium. Upregulation of angiogenic genes, VEGF, IL-8 and PROK-2[145], has been associated with aneurysm development and rupture. It has also been shown that inhibition of ***ets-***, an essential transcription factor for angiogenesis and a potential upstream pharmacologic target for MMP-9, results in the prevention of AAA progression in an elastase-induced rat model of this condition[146].

1.10 Apoptosis

The medial layer of AAA tissue shows decreased VSMCs density and increased apoptosis[147;148].

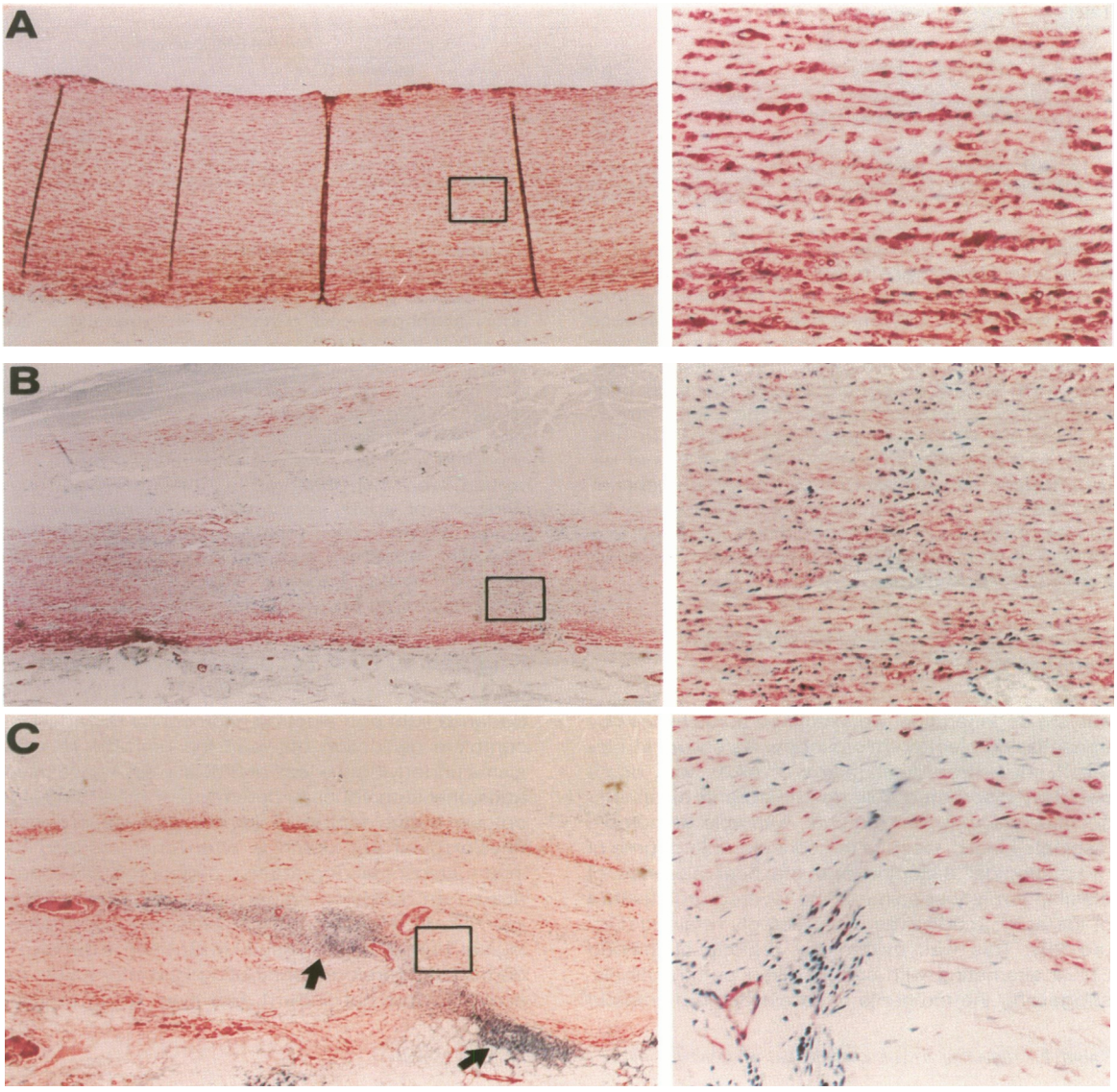


Figure 1.7 VSMCs stained with anti-α-SMC actin monoclonal antibodies in A. Normal aorta B. AOD and C. AAA. The abundance of SMC in the media of normal aorta and AOD is contrasted with decrease in medial SMC in AAA (arrow)[147].

Initiation of apoptosis occurs through either an intrinsic or extrinsic pathway, leading to activation of caspases that regulate DNA degradation[149]. The extrinsic pathway involves inflammation mediated by macrophages, lymphocytes and death ligands. The intrinsic pathway is secondary to DNA instability and oxidative stress[149]. Fas, its ligand FasL, perforin and elevated cellular production of p53 and p21 have been implicated in inflammation-mediated apoptosis in AAA[150]. Other mechanisms involved in apoptosis of VSMCs in AAA include: overexpression of TGF-β1[150] and inhibition of Rho-kinase, a key activator of apoptosis[151].

VSMCs contribute to vascular tone and synthesis of extracellular matrix. They also limit proteolysis by confining inflammation to the aortic adventitia[152]. Their depletion can promote AAA formation through elimination of a cell population that is capable of connective tissue repair.

1.11 Atherosclerosis and AAA

Atherosclerosis is invariably associated with the development of AAA because of the consistent finding of atheroma in the walls of the aneurysms[153]. This view has been challenged in recent years.

i) Atherosclerosis is a major risk factor for athero-occlusive disease and not all patients with atherosclerosis develop aortic aneurysm.

ii) Atherosclerosis is an intimal disease, whereas in the abdominal aorta, aneurysms are caused by medial damage.

iii) AAA is familial, under genetic influences and is unrelated to the lipid-related risk factors associated with atherosclerosis[154].

iv) Experimental models of hyperlipidemia in rabbits produce extensive aortic atherosclerosis but do not result in aneurysm formation in the aorta[155].

1.12 Oxidative Stress Theory

Reactive oxygen species (ROS) are formed during normal metabolism but their formation is increased under stress conditions such as localised inflammatory processes. The oxidative stress generated can result in progressive cell and tissue damage. ROS involvement in the pathogenesis of AAA is evidenced by reduced levels of antioxidants and increased lipid peroxidation in AAA wall when compared with normal aortic wall[156;157]. Potential sources of ROS include large numbers of infiltrating leukocytes (particularly macrophages), VSMCs, fibroblasts and endothelial cells that are all capable of forming superoxide via different pathways[158].

ROS can modulate the recruitment of inflammatory cells into the aortic wall of AAA by regulating the activities of cytokines and chemokines[159]. These inflammatory cells are important sources of proteolytic enzymes such as MMPs that are capable of degrading the aortic wall[160;161]. ROS play an important role in the pathogenesis of hypertension[162;163] which is an important risk factor in the development of AAA[164]. Another mechanism by which ROS can cause AAA development is through SMC apoptosis[165].

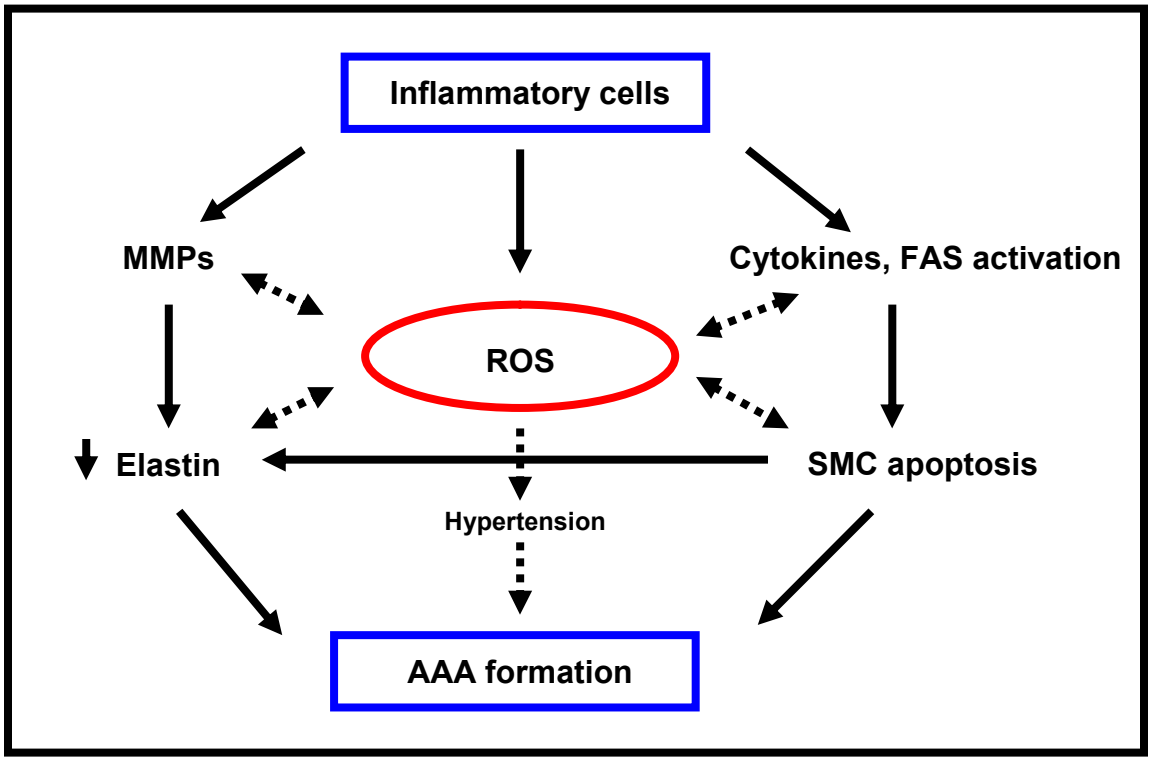


Figure 1.8 Mechanisms by which ROS may promote AAA formation. Proaneurysmal effects of ROS are shown in dashed lines[158].

1.13 Haemodynamic factors and biomechanical wall stress

The higher incidence of aneurysms in the infra-renal aorta compared with the thoracic aorta can be partly explained by its lower elastin concentration, reduction in its luminal diameter and an increase in turbulence caused by bifurcation of the aorta into iliac arteries[166]. The resultant turbulent flow can increase shear wall stress leading to aortic wall expansion[167].

The change in flow from laminar to turbulent has been shown to profoundly amplify the cellularity of experimental aneurysm wall[168] and to differentially regulate AAA gene expression[169]. There is an increase in intramural vascular inflammation, reduction in endothelial cell stability and production of reactive oxygen species[169].

Laplace law states that in a simple cylinder or sphere the wall tension (T) is equal to the pressure (P) times the radius (R) of the conduit i.e. $T = P \times R$. The risk of rupture increases with the size of the distension and the pressure within the sphere or cylinder. AAA formation is accompanied by an increase in wall stress and a decrease in wall strength which lead to further increases in the size of the AAA that eventually leads to rupture[170-172]. This simplistic model does not, however, explain why rupture occurs in about 3% of patients with a small aneurysm (i.e. < 5cm)[173]. AAA wall is complexly shaped with variable curvatures[174]. The wall stress is highly dependent on the shape (e.g. profile, tortuosity and asymmetry) of the specific AAA[175;176]. AAA of different diameters can have similar wall stress distribution making it difficult to predict wall stress without complex mathematical analysis (Figure 1.9).

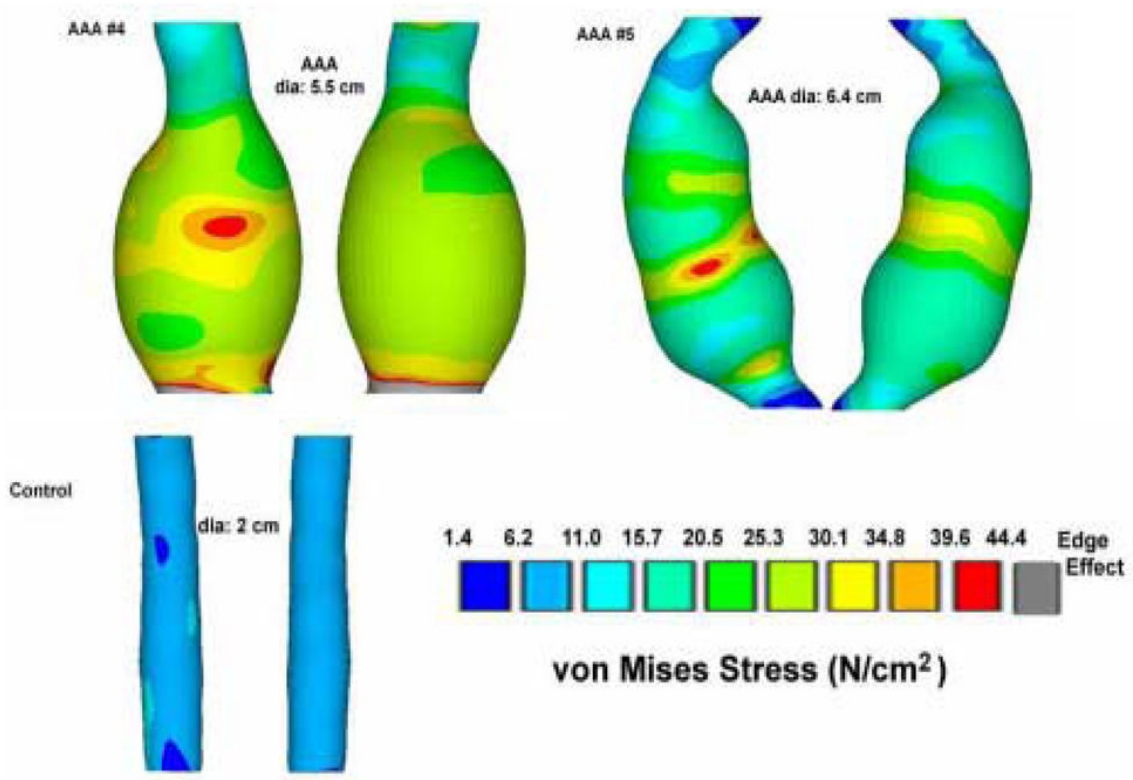


Figure 1.9 Wall stress distribution for 2 AAA and 1 nonaneurysmal aorta (bottom). Two views are shown for each aorta. Maximum diameter of top left AAA is 5.5 cm and top right is 6.4 cm. All subjects had normal blood pressure. Despite their differing sizes, peak wall stress was essentially similar in both AAA[177].

Most AAA walls are also lined by intraluminal thrombus (ILT) and its biomechanical behaviour should be considered in evaluating AAA wall stress. Ultrasound measures of ILT in AAA have shown that it is incompressible and undergoes non-linear strains[177]. ILT may therefore be mechanically protective by providing a cushioning effect to the AAA wall[177] (Figure 1.10).

Numerous formulae have been developed to predict AAA wall stress and possibly rupture. These models are however not ready for clinical application and patient management at this stage[177].

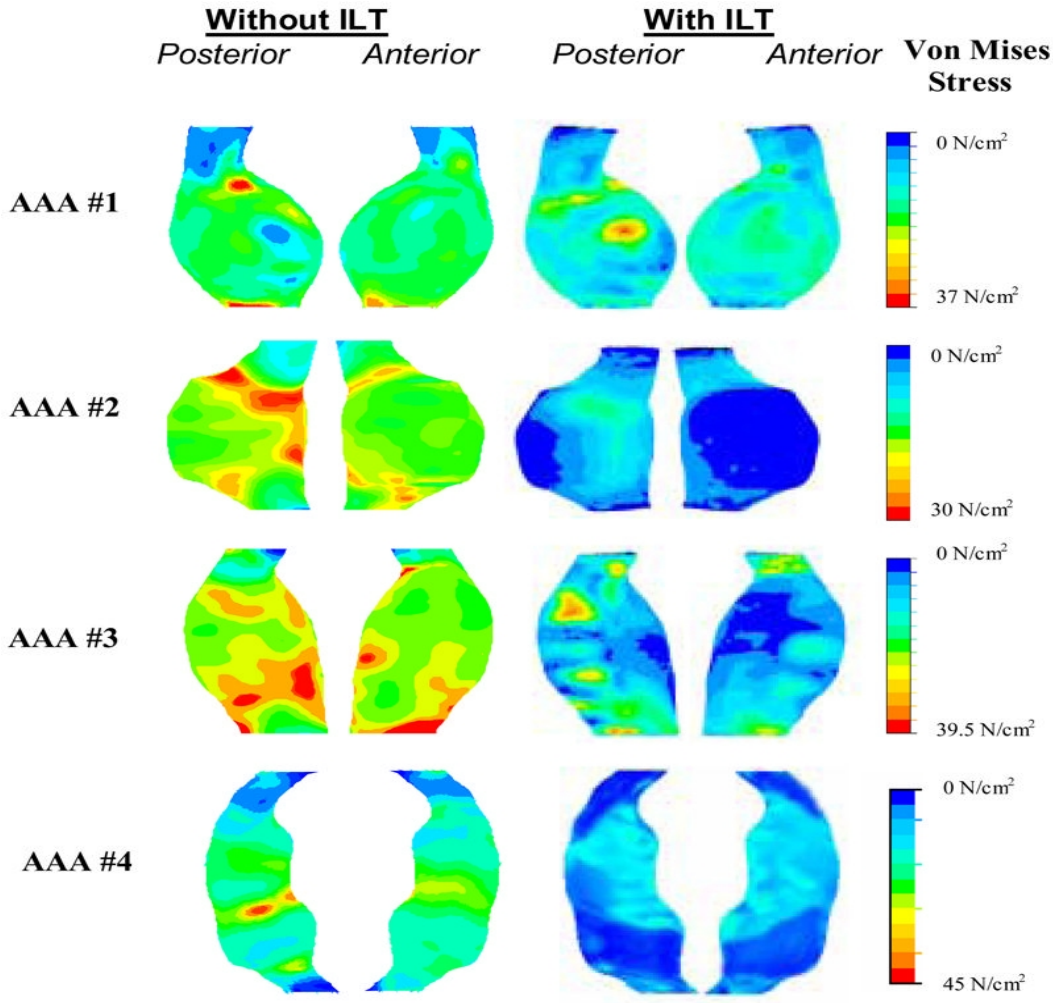


Figure 1.10 Comparison of 3D wall stress distribution between AAA model with and without ILT showing the cushioning effect of ILT[177].

1.14 Genetics of AAA

Abdominal aortic aneurysms are probably caused by a complex interaction between several genes and environmental factors, each of which has a different effect on disease susceptibility. A number of approaches have been used in an attempt to identify the disease-susceptibility genes in AAA. These include:

i) candidate gene studies;

ii) linkage studies;

iii) genomewide association studies;

iv) gene expression studies.

1.14.1 Candidate gene studies

The rationale behind candidate gene studies involves the selection of genes for investigation based on an educated guess and what is known about their roles in vascular biology. The major advantage of these association studies is that they are easy to design; they use independent patients who can be collected easily; and the mode of inheritance of the disease does not need to be specified. Two approaches have been described: DNA sequencing and single nucleotide polymorphisms (SNPs) as markers. In DNA sequencing, the coding, non-coding and promoter regions of a gene are sequenced in the patient's DNA to identify new variants. Most association studies however use SNPs as markers[178].

Plausible genes that have been studied in the context of AAA development are discussed below.

1.14.1.1 Genes in aortic wall structure

Elastin (ELN) Mutations in the ELN gene have not been found to be significant in abdominal aortic aneurysm in a study of 99 unrelated Italian patients with AAA[179]. The G/A polymorphism was found to be significant only in Canadian patients with a family history of AAA[180]. ELN mutations CL-16 and CL-13 were also found to be associated with thoracic aneurysm in patients with autosomal dominant cutis laxa[181]. From these studies, it can be concluded that ELN may play a role in familial AAA as opposed to sporadic AAA.

Collagen type 3A1 (COL3A1) COL3A1 is located on chromosome 2q31. In large studies, mutations of this gene have not been identified with sporadic or familial AAA[182]. A single base mutation in type III procollagen gene (glycine to arginine at position 619) was common among subjects in one family with AAA[179]. Variation between this SNP and AAA needs further investigation.

Fibrillin-1 Fibrillin-1 2/3 genotype is thought to be an important determinant of increased aortic stiffness in first degree relatives of patients with AAA[183]. This genotype variant is associated with hypertension and may explain the increased incidence of AAA[183;184]. The abnormal fibrillin may also weaken the structure of the aortic wall or affect the signalling of transforming growth factor beta

(TGFβ)[185], which is an important mediator of tissue remodelling. Mutations in TGFβ receptors type 1 or 2 can cause familial thoracic aortic aneurysm with dissection[186].

Fibulin-5 Fibulin-5 is an elastin binding protein[187] and its deficiency leads to fragmented elastin in mice[188]. Cutis laxa results from mutations in the fibulin-5 gene[189]. Due to its role in elastolysis, fibulin-5 gene is of interest in the pathogenesis of AAA. One genetic association study on AAA using three SNPs in the fibulin-5 gene showed no association with AAA[190].

1.14.1.2 Genes involved in remodeling of aortic wall

MMPs There are a number of polymorphisms in the genes for MMPs and their inhibitors TIMPs (Table 1.5). While some MMP polymorphisms have been associated with AAA, none of them have successfully predicted AAA expansion. The differing result with the MMP-9 polymorphism may be explained by the heterogeneity of different population groups.

Table 1.5 Candidate MMP and TIMP genes in AAA

Candidate gene	Association	Sample size	Populations
MMP-1	Association between single nucleotide polymorphism and AAA	22	Japan[191]
MMP-2	No association between -1306 C > T polymorphism and AAA expansion	455	UK[192]
MMP-3	No association between -1171 5A > 6A polymorphism and AAA expansion	455	UK[192]
	Association between single nucleotide polymorphism of MMP-3 and AAA	22	Japan[191]
	Association between 5A allele of MMP3 and AAA	47	Finland[193]
	Association between 5A allele of MMP-3 and AAA	405	UK[194]
MMP-9	No association between -1562 C > T polymorphism and AAA expansion	455	UK[192]
	Association between C-1526T polymorphism and AAA	414	New Zealand[195]
	No association between MMP9 polymorphism and AAA	47	Finland[193]
MMP-12	No association between -82 A > G polymorphism and AAA expansion	455	UK[192]
TIMP-1	Association between single nucleotide polymorphism of TIMP-1 and AAA	387	Belgium and Canada[180]
TIMP-2	No association between single nucleotide polymorphism of TIMP-2 and AAA	387	Belgium and Canada[180]
TIMP-3	Association between Single nucleotide polymorphism of TIMP-3 and AAA	387	Belgium and Canada[180]

Cysteine proteases There is no data regarding an association between cathepsin polymorphisms and AAA. Deficiency of cystatin C, the major extracellular inhibitor of cysteine proteases, is associated with increased aneurysm size and expansion rate[136]. Homozygosity for the A allele of cystatin C, associated with reduced cystatin C levels, is weakly associated with AAA growth[196].

Serine Proteases AAA wall contains significant levels of plasminogen activators (tPA and uPA)[134]. A single nucleotide polymorphism (4G>5G) in the gene expressing their main inhibitor, PAI-1, has been associated with raised PAI-1 expression for the 4G allele[197]. A study of 190 patients with AAA showed a higher frequency of the -675 5G insertion allele of the 4G>5G polymorphism in patients with familial AAA only[198]. Another study involving 460 unrelated patients failed to show a relationship between this polymorphism and AAA, but found that the 5G/5G genotype had the fastest aneurysm growth rate[199].

1.14.1.3 Genes of the cardiovascular system

ACE and Angiotensin II type I receptor (ATIR) genes Genes for angiotensin converting enzymes (ACE) and angiotensin II type I receptor are plausible candidate genes for AAA as they are expressed in human aneurysmal aorta[200] and their polymorphisms have been associated with other cardiovascular disease[201]. Increased angiotensin II levels may lead to remodelling of vascular tissue[202], but its role in aortic dilatation remains unknown. Possible mechanisms

include promotion of hypertension and altered shear stress[203], activation of growth factors and inflammation either through the induction of cytokines and VCAM-1 expression[204], or activation of NF-kβ-dependent gene expression[205].

A significant association between the ACE ID polymorphism and AAA was established in both normotensive and hypertensive patients, but no relationship was found with variants of the ATIR gene[206]. A similar association has been reported in 56 normotensive and 68 hypertensive patients with AAA[207]. The ACE polymorphism may therefore be a potential therapeutic target.

Apolipoprotein B (APOB), Apolipoprotein E (APOE) and Cholesterol Ester Transfer Protein (CETP) Both ApoB and ApoE are associated with increased risk of atherosclerosis. In a study investigating the association of the XbaI polymorphism of ApoB gene in patients with AAA with and without additional popliteal artery aneurysms, no differences in allele frequencies were reported[183]. ApoE knockout mice develop atherosclerosis and AAA after infusion with angiotensin II. The E2, E3 and E4 alleles of this gene were investigated in patients with small AAA. Though the E3/E4 genotype was associated with a significant decrease in AAA expansion rate compared with the E3/E3 genotype in a small study[208], these findings were however not replicated in a larger study[209]. There was no association between microsatellite polymorphism of the cholesteryl ester transfer protein gene (CETP) and AAA[210].

1.14.1.4 Genes involved in methionine metabolism

Methylenetetrahydrofolate reductase (MTHFR) A mutation in the MTHFR gene is associated with increased levels of homocysteine[211] which results in increased elastolytic activity in the arterial wall and possible AAA formation[212]. Two studies including 58 Italian patients[213] and 63 Polish patients [214] with AAA showed an association between the C677T allele of the MTHFR gene and AAA development. This was not, however, reproduced in a later New Zealand study involving 428 AAA patients[215].

Other genes coding for enzymes involved in methionine metabolism Giusti et al.[216] investigated 56 polymorphisms in 17 candidate genes involved in methionine metabolism in patients with AAA (n=423) and controls (n=423). After adjustment for cardiovascular risk factors and chronic obstructive airway disease, a significant association was found between AAA and haplotypes of adenosylhomocysteinase (AHCY), folate hydrolase (FOLH1), methylenetetrahydrofolate dehydrogenase 1 (MTHFD1), 5-methyltetrahydrofolate-homocysteine methyltransferase (MTR), nicotinamide-N-methyltransferase (NNMT), paraoxonase 1(PON1) and thymidylate synthetase (TYMS). These results need to be confirmed in a larger study.

Haptoglobin Three studies have investigated the association of the haptoglobin gene variant and AAA. Two small studies involving 28 families[210] and 52 patients[217] with AAA showed no association with the haptoglobin gene variant. A

larger study involving 83 patients[218] showed that the HP 2-1 genotype was associated with increased AAA expansion compared with HP 1-1 and HP 2-2 genotypes. Serum elastase activity and CRP levels were also higher in patients with HP 2-1 genotype.

1.14.1.5 Genes involved in inflammation

Inflammation is an important pathophysiological process in AAA development[92]. Inflammatory cells including leukocytes, macrophages and plasma cells capable of releasing a number of cytokines have been immunolocalised in AAA wall[92]. Several inflammatory-related genes have thus been investigated in AAA.

Interleukins Interleukin-1, -6 and -10 have been studied in AAA. IL-1 regulates inflammatory pathways, is involved in extracellular matrix remodelling through induction of MMPs and promotes VSMCs apoptosis. However, no association has been found between polymorphisms in IL-1 gene and AAA. IL-6 is a pro-inflammatory cytokine. Though increased levels of interleukin-6 have been identified in patients with AAA, no association has been found with the -174 G/C polymorphism of the interleukin-6 gene[219]. IL-10 is an anti-inflammatory cytokine and the G-allele instead of the A–allele has been associated with a reduction in IL-10 production[220]. No association of either allele with AAA was found[221].

Chemokines Chemokine receptor 5 (CCR5) is associated with atherosclerotic disease[222]. A higher frequency of a 32 base pair deletion in the CCR5 gene allele

has been shown in AAA patients compared with patients with atherosclerotic disease[223]. However, there was no difference in this allele between AAA patients and controls[224].

Human Leukocyte antigen locus (HLA-), Tumour Necrosis Factor (TNF) and PPAR-γ No significant association has been found between the HLA genes and AAA[225]. TNF is a pro-inflammatory cytokine whose expression is increased in individuals with the A-allele compared with those with the G-allele[226]. However, a genetic association study showed no association between the A-allele and patients with AAA[227]. PPAR-γ downregulates the expression of osteoprotegerin (OPG) in mouse model[228]. Levels of OPG are increased in aortic biopsies[229]. Two polymorphisms in the PPAR-γ gene were studied in 4227 men out of whom 699 had an AAA[230]. PPAR-γ 1347C>T polymorphism was associated with increased AAA growth.

1.14.1.6 Genes involved in signalling pathways

Transforming growth factor β (TGFβ) Variants in TGFβ1, -2, -3 and their receptors lead to VSMCs apoptosis and thus may be involved in AAA development[231]. Mutations in TGFβ receptor are associated with thoracic aortic aneurysm[186]. No association has been found between TGFβ1 or its receptor and AAA[231;232]. Two large case-control studies[232;233] showed an association between two SNPs (rs1036095 and rs4522809) of TGFβ-2 receptor and AAA. Polymorphisms in TGFβ3 and its receptor were not associated with AAA[234].

Oestrogen receptor 1 and 2 and Progesterone receptor The incidence of AAA is higher in man and post-menopausal women. Thus the sex hormones may play a role in AAA development. Oestrogen receptor-1 and -2 and progesterone receptor (PGR) variants were not associated with AAA.[235;236]

Most of the candidate gene studies described above do not have sufficient samples to detect statistically significant association between a particular gene variant and AAA. Sporadic and familial AAA also seem to have different predisposing genes. Study design is further compounded by the genetic heterogeneity expressed in AAA tissues in patients from different population groups.

1.14.2 Linkage studies

Genetic linkage studies identify relationships between the chromosomal location of known genes and disease phenotype in families in which the disease segregates. The entire genome is analysed. They are of limited use in AAA as in most cases only one generation is affected because the parents have died or the children are too young to have developed AAA. The presumed mode of inheritance also needs to be defined, which in AAA is likely to be heterogeneous[237]. To overcome some of these problems, an affected sib-pair analysis can be carried out[238].

A major locus for familial AAA was mapped to chromosome 19q13.3 in three Dutch families with familial AAA[239]. No evidence of linkage to this chromosome was however detected in a further analysis of 101 affected sib-pairs in the same study. Linkage analysis involving patients from different countries identified chromosomes 19q13 (LOD score 4.75, p=0.00014) and 4q31 (LOD score 3.73, p=0.00012) as possible loci for AAA[240]. Although chromosome 19q was mapped in both studies, the loci did not overlap. This possibly reflects the genetic heterogeneity indicating that at least 2 different genes may be responsible in AAA. These regions are candidate regions for AAA susceptibility genes and the specific disease-causing gene polymorphism(s) now needs to be identified. Linkage of 19q13 has also been made with intracranial aneurysmal disease in a cohort of Finnish patients[241]. Plausible candidate genes on chromosome 19q13 that may have a role in AAA development include: plasminogen activator urokinase receptor (uPAR), which has a role in the localised degradation of the extracellular matrix and whose levels are raised in AAA wall[134] ; calpain 12 (involved in SMC apoptosis)[242] and LIR9 (cross-linking of LIR9 on monocytes causes the release of inflammatory cytokines IL1B, TNF-alpha and IL-6 [243] that may be important in the inflammatory process in aneurysmal wall).

A recent association study using SNPs of common genetic variants on chromosome 19q13 in two independent case-control sets showed no differences in allele frequency in patients with AAA and controls. This can be explained by the fact that sporadic and familial AAA may have different genetic basis[244].

1.14.3 Genomewide association studies

Genomewide association study (GWAS) is an unbiased approach of studying the association between markers i.e. SNPs across the genome and disease. This approach is hypothesis free (i.e. there is no existing hypothesis about the association between a disease and a particular gene or locus)[245]. Three GWAS on AAA has been reported.

The first GWAS[246] for AAA was carried out using pooled DNA samples from 123 AAA cases and 112 controls matched for age, gender and smoking history using Affymetrix 500K SNP arrays. A candidate AAA-associated haplotype was identified on chromosome 3p12.3. Four SNPs in this region were strongly associated with AAA on individual genotyping. One SNP in this region (rs7635818) located near the contactin-3 gene was confirmed in a larger sample size and the association was even greater in smokers who are at high risk of developing AAA. This study is however underpowered and a further study[247] genotyping the rs7635818 in 567 patients with AAA and 552 controls could not confirm any association.

The second GWAS on AAA identified an association between the A allele of rs7025486 located within the DAB2IP gene on chromosome 9q33.2 and AAA[248]. This association was also found with other vascular diseases such as early onset myocardial infarction, peripheral arterial disease and pulmonary embolism but not with intracranial aneurysm or ischaemic stroke. There was no association

between this SNP and common risk factors for vascular diseases such as smoking, lipid levels, obesity, type-2 diabetes or hypertension.

The most recent GWAS on AAA was carried out with 1866 patients with AAA and 5435 controls and replication of promising signals in 2871 additional cases and 32,687 controls and performed a further follow-up study of 1491 AAA and 11,060 controls[249]. In the discovery study, nine loci were found to be associated with AAA. In the replication stage the lead SNP at one of these loci, rs1466535, located on chromosome 12q13.3 showed significant association with AAA and this was confirmed on the follow-up study. The rs1466535 is located within intron 1 of the low-density-lipoprotein receptor-related protein-1 (LRP-1). No association was seen between rs1466535 and the 12q13.3 locus in independent association studies of coronary artery disease, blood pressure, diabetes or hyperlipidaemia, suggesting that this locus is specific to AAA[249]. The C allele of the rs1466535 demonstrated a trend towards increased expression of LRP-1 gene. The rs146635 is a biologically plausible genetic variant specifically associated with AAA.

The main weaknesses of genomewide association studies are that a large number of common variants are identified and most of them have a modest effect in influencing the disease. Their real strength however lies in the discovery of novel biologic pathways underlying the pathogenesis of AAA.

1.14.4 Gene expression studies

These studies can identify the differential expression of genes in AAA wall compared with wall obtained from normal and occluded aorta.

Analysis using a limited gene microarray platform has revealed only 44 of 1176 genes investigated (3.7%) to be differentially expressed in AAA wall compared with wall from normal aorta[135]. Genes that were consistently upregulated with the greatest-fold increase were: myeloid nuclear cell differentiation antigen, cathepsin H, platelet-derived growth factor A, apolipoprotein E, MMP-9 and interleukin-8. Genes that were consistently down regulated were myosin light chain kinase and β1 integrin. This pattern of gene expression reflects chronic inflammation, extracellular matrix degradation, atherosclerosis and smooth muscle cell depletion.

A smaller microarray chip set analysis comparing gene expression in wall from AAA, AOD and normal aorta has revealed a similar proportion of differentially expressed genes between AAA and AOD (11 of 265, 4.1%)[250]. Three were down regulated in AAA: collagen VI αI, glycoprotein IIIA and alpha2 macroglobulin and three were upregulated in both AOD and AAA: MMP9, ICAM-1 and TNFβ receptor. Three genes were down regulated in both AOD and AAA: integrin α5, ephrin α5, and rho/rac guanine nucleotide exchange factor. Only MMP9 was significantly upregulated in both AAA and AOD of the 16 MMPs evaluated.

Evaluation of three of the TIMPs showed no significant expression for all tissue types although TIMP-1 tended towards upregulation in AAA.

Comparison of gene expression in infra-renal AAA, with thoracic aneurysms and normal aorta again using a limited microarray of 1185 genes[95] found that of 8 gene products that were significantly differentially expressed between AAA and thoracic aneurysms only 4 were directionally concordant (MMP 9, v-yes-1 oncogene, mitogen-activated protein kinase 9, and intercellular adhesion molecule 1/CD54). MMP-9, CD86/B7-2 antigen, bystin-like, apolipoprotein E, integrins β2 and β8, non-receptor tyrosine kinase 1, Janus Kinase 3, IL-8 and PKC-σ were differentially expressed when comparing AAA with normal aortic wall.

Comparison of normal aorta with AAA in two studies using different microarray platforms[95;135] that interrogated a variable number of transcripts (1176 and 1185 respectively) has revealed a similar differential expression profile of genes. These included Cathepsin H, ApoE, MMP-9, IL-8, CXCR4, Decorin, RANTES, MLCK and ICAM-1. Of these, MMP-9, ApoE and ICAM-1 were, however, found to be equally upregulated in AOD and AAA compared with normal aorta, confirming the mRNA expression studies[250], which suggest these factors are mediators of atherosclerosis rather than aneurysmal disease development[123]. The differential expression of cathepsin H at the protein and activity level (in AAA versus AOD) has been recently confirmed[133].

Of the genes located on chromosome 19q13, only GRLF1 (a factor regulating endothelial vascular permeability) was found to be upregulated in AAA compared with normal wall[251].

These findings need to be confirmed using a whole transcriptome approach that compares AAA, AOD and normal aortic wall. This may help to elucidate novel genes that are specifically up or down regulated in the aneurysmal wall and are not associated with atherosclerosis.

1.15 Hypothesis and Aims

1.15.1 Hypothesis

AAA is a polygenic disorder. To date, only focused gene expression studies have been carried out to identify genes that might be important in AAA development. The only genomewide array has looked at differential gene expression in AAA rupture compared with the wall of normal aorta[145]. These studies are limited and have not screened for genes that are located on chromosome 19q13 that has been identified as a susceptible locus[240]. A comprehensive genomewide analysis will provide the full profile of differentially expressed genes that could reveal novel genes that are important in AAA development.

1.15.2 Aims

1. To characterise the gene expression signature in AAA, AOD and NA using a genomewide scan.

2. To identify the genes that are differentially expressed on the two chromosomal loci (19q13 and 4q31)[240] that have been the most strongly linked to AAA. These are the only two linkage studies published at the time this experiment was carried out.

3. To confirm the differential expression of consistently expressed genes at the transcription level (using quantitative real-time polymerase chain reaction, qRT-PCR) on a larger sample size.

4. To carry out bioinformatics analysis in order to identify molecular pathways that may be involved in AAA.

Chapter 2

RNA EXTRACTION AND QUALITY CONTROL

2.1 Introduction

2.1.1 RNA and its extraction

Ribonucleic acid (RNA) is composed of nucleic acids that are found in the nuclei of plants and animals. Nucleic acids consist of high molecular weight macromolecules that are made up of smaller single units called nucleotides. RNA represents the genetic traits of an organism and determines phenotypes through translation into protein.

Each nucleotide molecule consists of a sugar group, a phosphate group and an amino group. There are only four bases that make up RNA: adenine, cytosine, guanine and uracil (A, C, G and U respectively). Structurally, the backbone consists of alternating sugar and phosphate parts, while the amino groups protrude like branches from the backbone (Figure 2.1) [252].

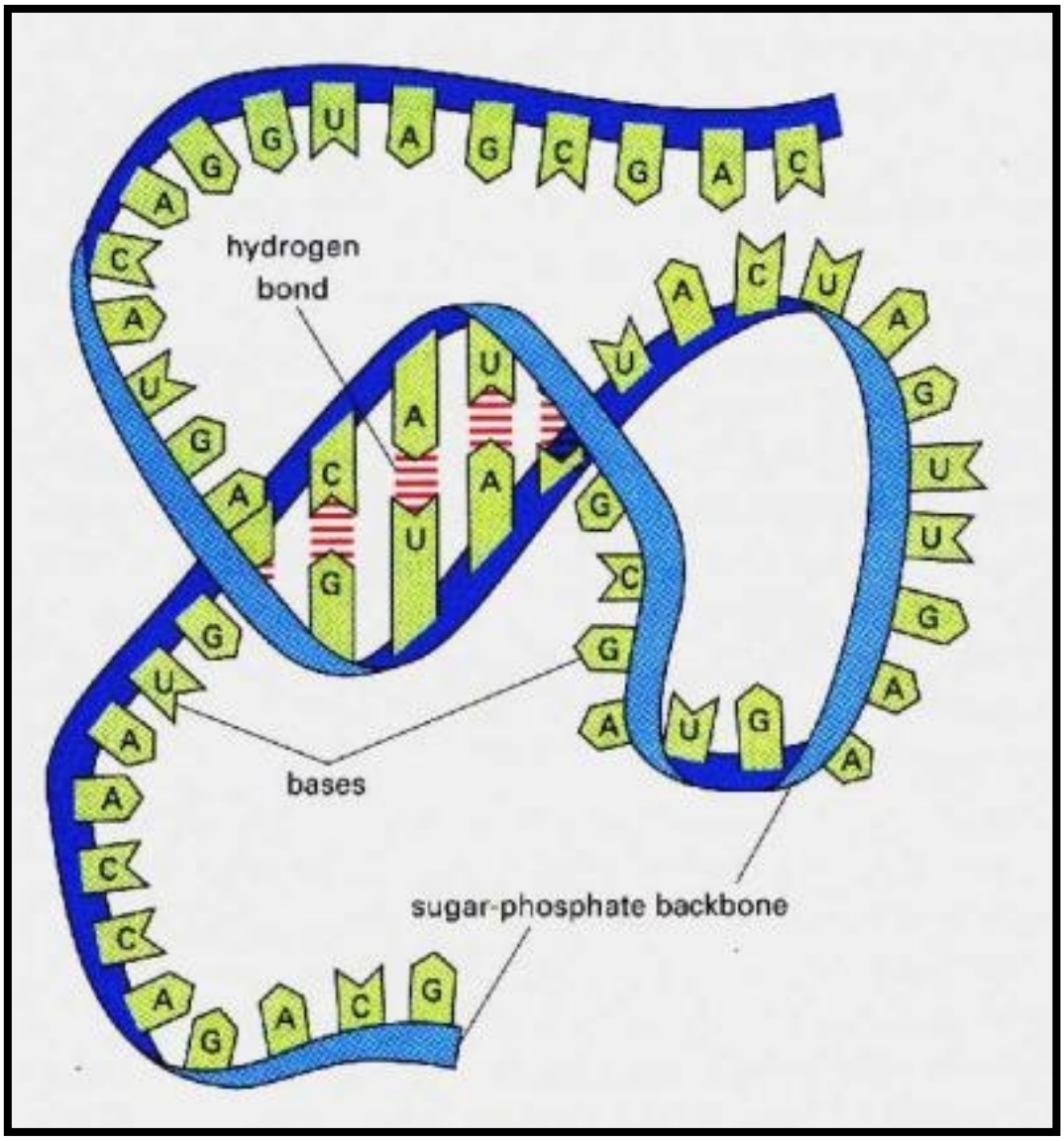


Figure 2.1 Structure of RNA[253].

Successful RNA extraction and purification involve 3 steps[252]:

i) effective disruption of cells or tissue;

ii) denaturation of nucleoprotein complexes;

iii) inactivation of nucleases that is capable of degrading the RNA.

RNA is an unstable molecule, having a very short half-life once extracted. There are two methods of RNA extraction: conventional method and solid phase extraction.

2.1.1.1 Liquid phase extraction. The guanidinium-thiocyanate-phenol-chloroform extraction method is a single step technique first described by Chomczynski and Sacchi[254]. RNA is separated from DNA and protein using a solvent/aqueous phase separation.

2.1.1.2 Solid phase RNA extraction. This method of RNA extraction is used by most commercial extraction kits. It allows quick and efficient purification compared with conventional methods. Glass particles, silica matrices and anion-exchange carriers can be used as solid or selective adsorption surface. The sample is first digested using a lysis buffer and the digest applied to a spin column which has been conditioned for adsorption using a buffer at a particular pH. RNA will adsorb to the column with the aid of the high pH and salt concentration of the binding solution. Other contaminants which may bond to the column surface are then removed using a washing buffer containing a competitive agent. RNAse free water is then used to elute the RNA from the column in the purified state[255].

2.1.2 RNA QUALITY CONTROL

Traditionally, RNA integrity has been determined using agrose gel electrophoresis stained with ethidium bromide. This typically shows 2 bands comprising of the 28S and 18S ribosomal RNA (rRNA) species and other bands where smaller RNA species are located. RNA is considered of high quality when the ratio of 28S:18S is about 2.0 [256]. This approach has two disadvantages:

(i) it requires a relatively large volume (5µl) of potentially precious sample;

(ii) it is subjective, in that the gel images rely on human interpretation making comparisons from one laboratory with another difficult.

2.1.2.1 Bioanalyser 2100 (Agilent).

The bioanalyser uses the same principle as gel electrophoresis. Each RNA chip contains an interconnected set of microchannels that is used for separation of nucleic acid fragments. Tiny amounts of RNA samples (10µl) are separated in the channels according to their molecular weight and subsequently detected via laser-induced fluorescence detection. The results are visualised as an electropherogram (Figure 2.3) where the amount of measured fluorescence correlates with the amount of RNA of a given size.

Figure 2.2 Bioanalyzer 2100 (Agilent technologies).

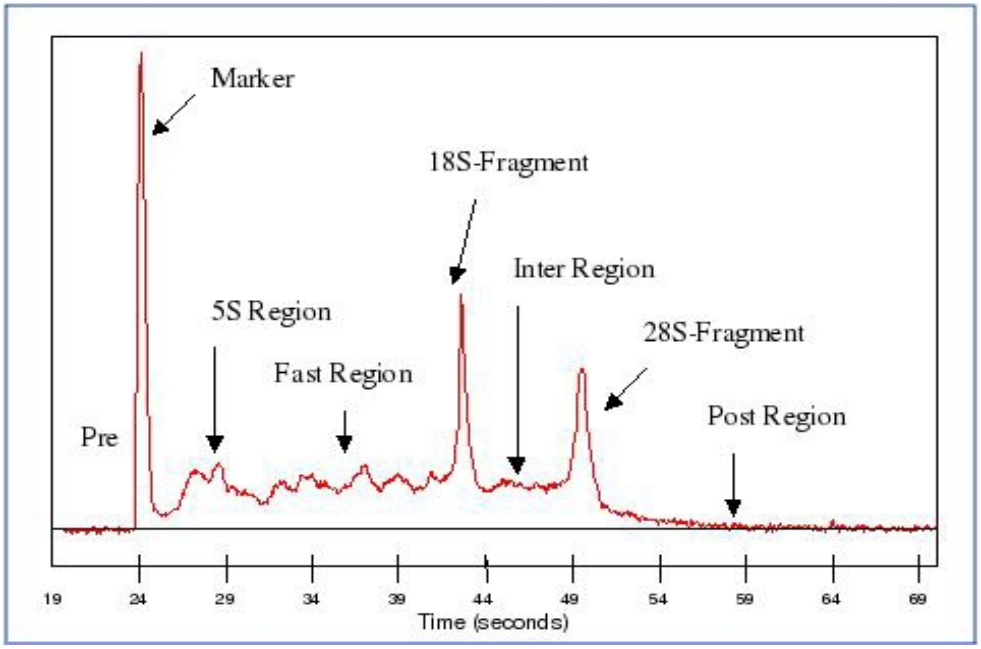


Figure 2.3 Electrophoregram from the bioanalyser. The segment preceding the lower marker is designated the pre-region. The 5S region covers the small rRNA fragments. The 18S and 28S represent the main RNA ribosomal peaks256.

The quality of the RNA is assessed by the 28S:18S ribosomal ratio and the RNA integrity number (RIN). The RIN number is generated by the software using methods to rank features according to their informative content and using a Bayesian approach to select and train a prediction model on the basis of artificial neural networks[256]. RIN value is assigned a number from 1 (totally degraded RNA) to 10 (pure RNA) (Figure 2.4). The following features are taken into account when assigning a RIN value[256]:

i) *The total RNA ratio.* This is the fraction of the area in the region of the 18S and 28S compared with the total area under the curve. This reflects the proportion of large molecules compared with smaller ones. The higher the ratio is the smaller is the RIN number.

ii) *The height of the 28S peak*. The 28S band disappears faster during RNA degradation than the 18S band and therefore it allows detection of a beginning of degradation.

iii) *The fast area ratio*. This reflects the degree of RNA degradation.

iv) *The marker height*. The value will be higher for degraded RNA compared with pure RNA.

Based on the following features, the value generated by the RIN number has been shown to be a more consistent and reproducible method of assessing RNA quality between laboratories.

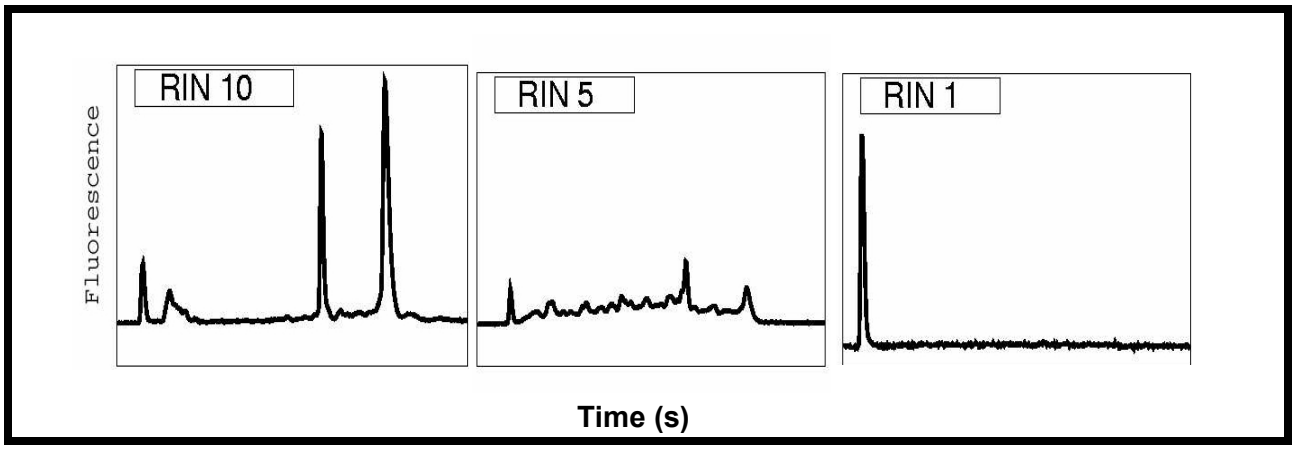


Figure 2.4 Electrophoregrams of RNA at different stages of degradation ranging from 10 (pure RNA) to 1 (totally degraded RNA) [256].

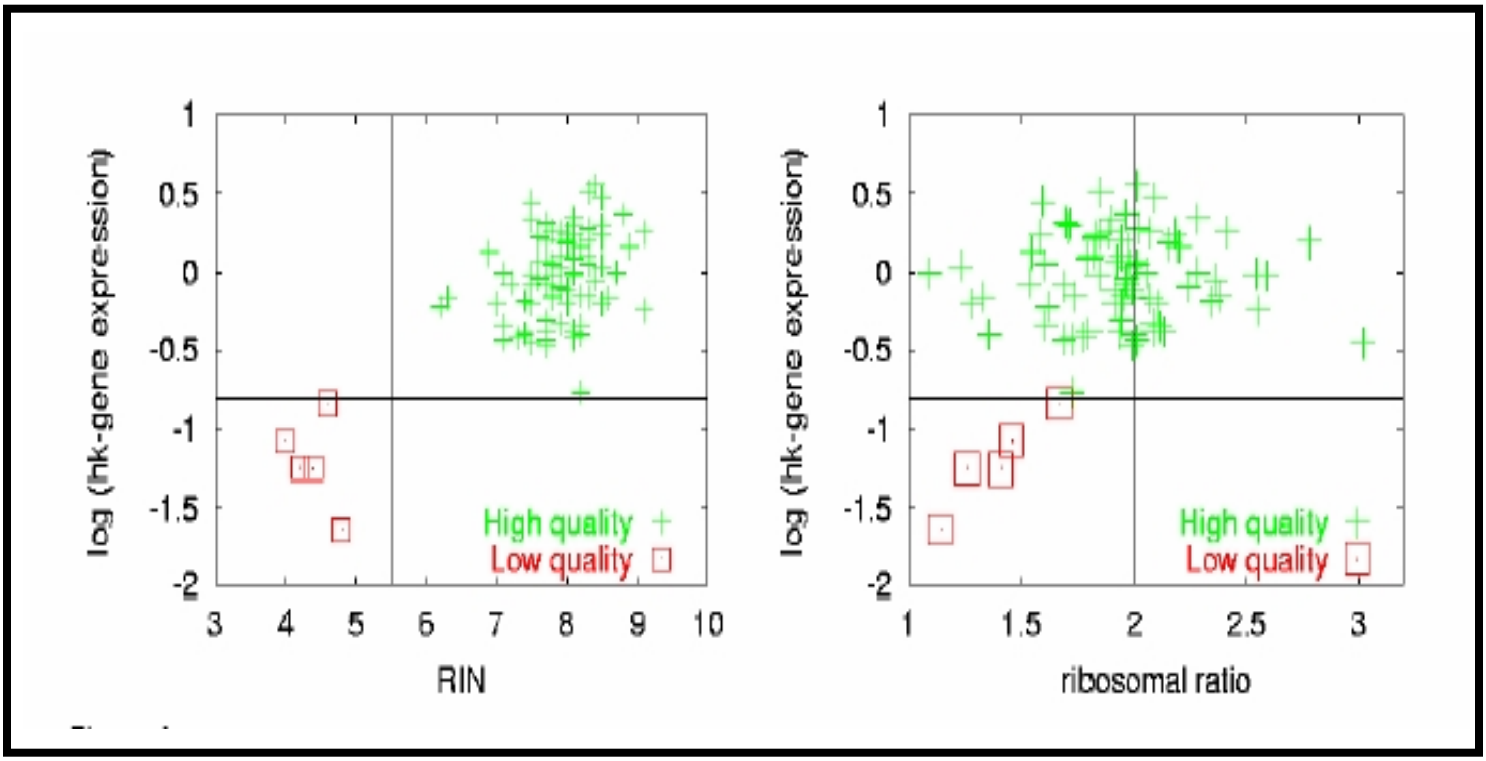


Figure 2.5 Correlation between RIN and 28S:18S ratio against average expressions of housekeeping genes[256].

Figure 2.5 shows a number of RNA samples with varying RIN values and ribosomal ratios and their average expressions of 4 housekeeping genes (GAPDH, KYNF, NEFL, β2M) in an RT-PCR experiment. RNA samples of high quality will show high expression of housekeeping genes. A RIN value > 5.5 is more sensitive and specific than a ribosomal ratio of 2.0 or higher as determined by gel electrophoresis at identifying RNA of high quality[256].

2.1.2.2 Nanodrop

The Nanodrop ND-1000 is a full spectrum (220-750 nm, Figure 2.6) spectrophotometer that uses sample retention technology that employs surface tension alone to hold the sample in place. It accurately measures RNA concentration and purity[257]. It has the following advantages over the conventional spectrophotometer with cuvette:

i) it uses only 1µl of the sample as opposed to 5µl;

ii) it is less cumbersome and time consuming to set up;

iii) it can measure samples with high concentration accurately without dilution.

Figure 2.6 Nanodrop ND-1000

RNA extract is placed on one end of a fibre optic cable. A second fibre optic cable is then brought into contact with the liquid sample bridging the gap between the fibre optic ends. A pulsed xenon flash lamp provides the light source. The light passing through the sample is analysed using a

spectrometer utilising a CCD array[257]. The concentration of the nucleic acid and the absorbance at 260 and 280nm are displayed. The ratio of the absorbance at 260 and 280nm is used to assess the purity of the RNA. A ratio of approximately 2.0 indicates pure RNA. If the ratio is appreciably lower, it indicates the presence of proteins, phenol or other contaminants that absorb strongly at 280nm[257] (Figure 2.7).

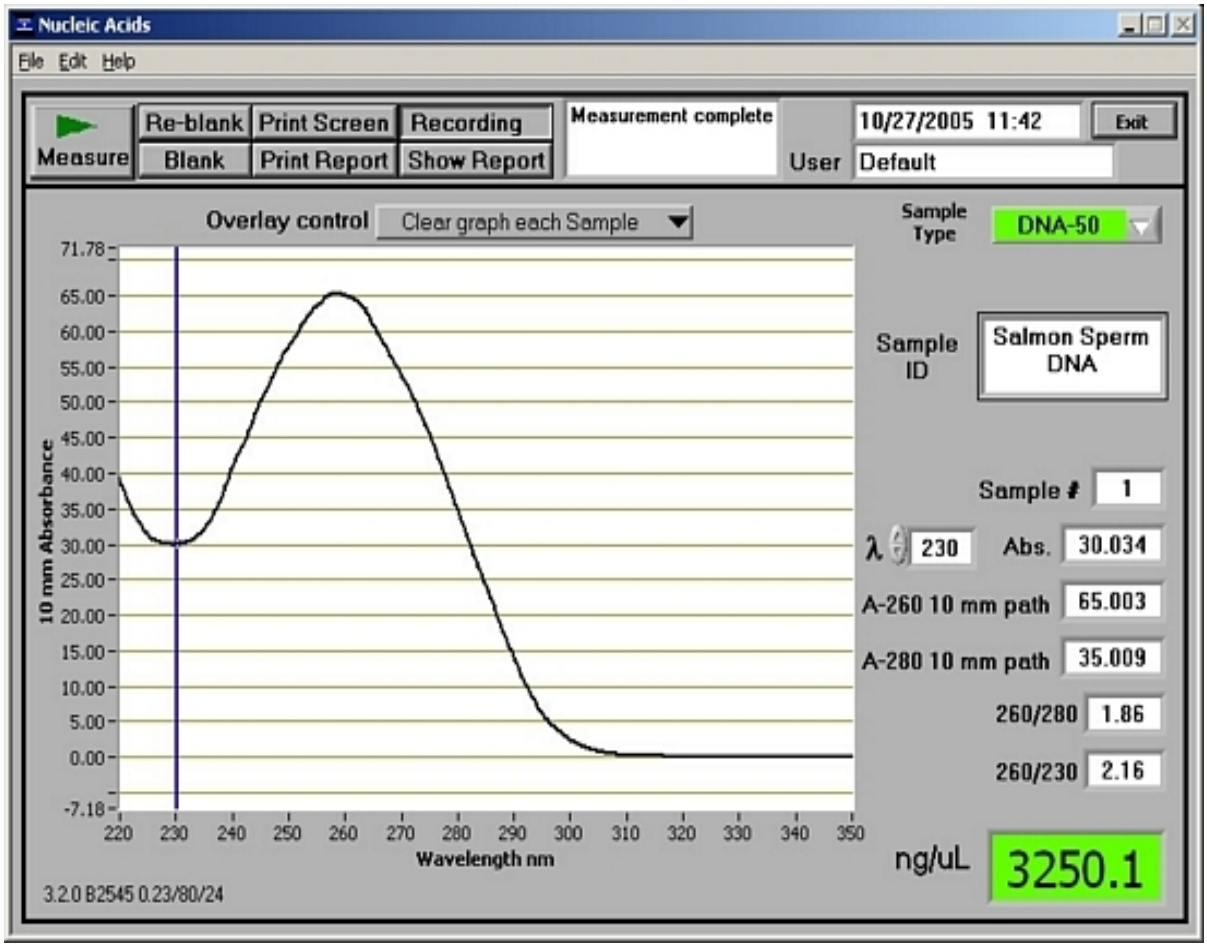


Figure 2.7 Example of spectrum display for nucleic acids using the Nanodrop, ND 1000.

2.2 Material and Methods

2.2.1 Samples used

AAA and AOD cases were identified during their outpatient visits at St Thomas's Hospital. Informed consents for blood samples and aortic tissues were obtained from all the patients by the research fellows during their inpatient stay prior to their surgery. All samples were collected under the approval of the ethics committee responsible for Guy's and St Thomas NHS trust. All AAA cases were confirmed either on ultrasound scan or computed tomography scan. AOD cases were confirmed on peripheral angiograms. Relevant data including date of collection, time between collection of tissues from theatre to being snap-frozen in liquid nitrogen (only for samples collected by myself), patients' demographics, co-morbidities, smoking history and size of aneurysms were duly recorded in a database.

Normal infra-renal aorta was obtained from the tissue bank at the UKHTB, Leicester, UK. The tissues were obtained from cadaveric donors under the approval of their ethics committee. The time to processing of those tissues were prolonged.

2.3 RNA EXTRACTION

2.3.1 Tissue preparation

Aortic walls were obtained from 27 patients with AAA (labelled AAA1-AAA27) and 17 patients with AOD (labelled AOD1–AOD17). A 1×3 cm strip of wall was taken from the middle anterior sac during aneurysm repair, and a small sample of wall was taken from the arteriotomy site during AOD repair. A sample of normal infra-renal aortic wall was also collected from 10 normal subjects (labelled NA1-NA10) (obtained from the tissue bank at the UKHTB, Leicester, UK). The study flow for samples used in each group (i.e. AAA, AOD and NA) in the microarray and qRT-PCR studies is shown in Figure 2.8.

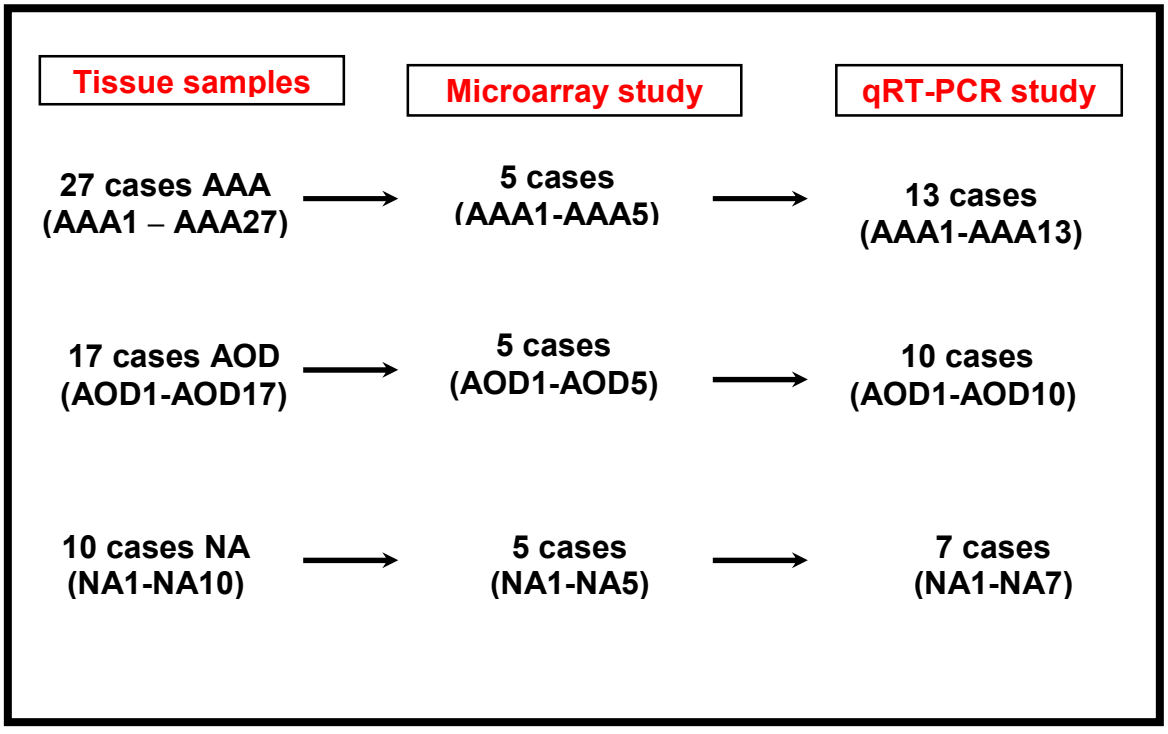


Figure 2.8 Study flow diagrams.

The tissue was washed with sterile Dulbecco's phosphate buffered saline (D-PBS), ph 7.4, to remove clots and blood in order to prevent contamination from blood components. The tissue was cut into 5mm squares, snap-frozen in liquid nitrogen and stored at -80ºC to prevent RNA degradation.

2.3.2 Tissue homogenisation and RNA extraction

All RNA extractions and subsequent experiments for all the samples were done by me. Polytetrafluoroethylene (PTFE) cups and stainless steel ball bearings were autoclaved twice to reduce any RNAse activity and pre-cooled in liquid nitrogen for about 20 minutes to minimise RNA degradation during homogenisation. Tissue (~100mg) was homogenised using the Micro-Dismembrator S (Sartorius) at 3000rpm for 1 minute. This 'ball-milling' method breaks up the frozen tissue into powder. Trizol reagent 1ml, (GIBCO, BRL, UK) was added to the frozen powder and the mixture further homogenised for 30 seconds, at 3000rpm on the Micro-dismembrator. The homogenate was allowed to stand for 10 minutes at room temperature, before being transferred to a sterile polypropylene, conical Eppendorf microtube. Chloroform (Molecular Biology Grade, Sigma) was added to the mixture at a volume of 0.2ml per 1ml of Trizol used. The tube was shaken vigourously by hand for 20 seconds and allowed to stand on ice for 5 minutes. Following centrifugation at 3000rpm for 20 minutes at 4ºC, the colourless upper aqueous phase was then recovered taking care not to contaminate it with the white DNA interphase.

2.3.3 RNA purification

Two methods of RNA purification were compared.

2.3.3.1 Precipitation with isopropanol The aqueous phase containing the RNA was mixed with 0.5ml of isopropanol (Molecular Biology Grade, Sigma) per ml of Trizol used for the isolation. This was mixed by inversion and allowed to stand for 10 minutes. Precipitation of the pellet containing the RNA was obtained after centrifugation at 3000rpm. The pellet was washed with 70% ethanol (Molecular Biology Grade, Sigma) air dried for about 10 minutes, reconstituted with 20µl of RNAse free water (Qiagen, UK) and snap frozen and stored at -80ºC.

2.3.3.2 Purification with RNEasy kit (Qiagen) The aqueous phase was mixed with an equal volume of 70% ethanol and mixed by pipetting. The sample was applied to an RNA Midi Column (Qiagen) and passed through the column by centrifuging for 5 minutes at 1500rpm and room temperature (Figure 2.9). The column was washed with buffer RW1 from the Midi Column kit. DNAse digestion was carried out by pipetting 160µl of DNAse I mix (Qiagen) directly on the RNeasy column and allowed to incubate at 20-30ºC on the bench top for 15 minutes. This optional step was added in order to decrease possible contamination with genomic DNA, which could affect the specificity and sensitivity of both the micro-array and subsequent qRT-PCR analysis. The column was given a further wash using buffer RW1, followed by two successive washes with buffer RPE from the same kit. The RNA was eluted from the column

by addition of 150µl of RNAse free water (Qiagen, UK). The RNA was snap-frozen and stored at −80ºC.

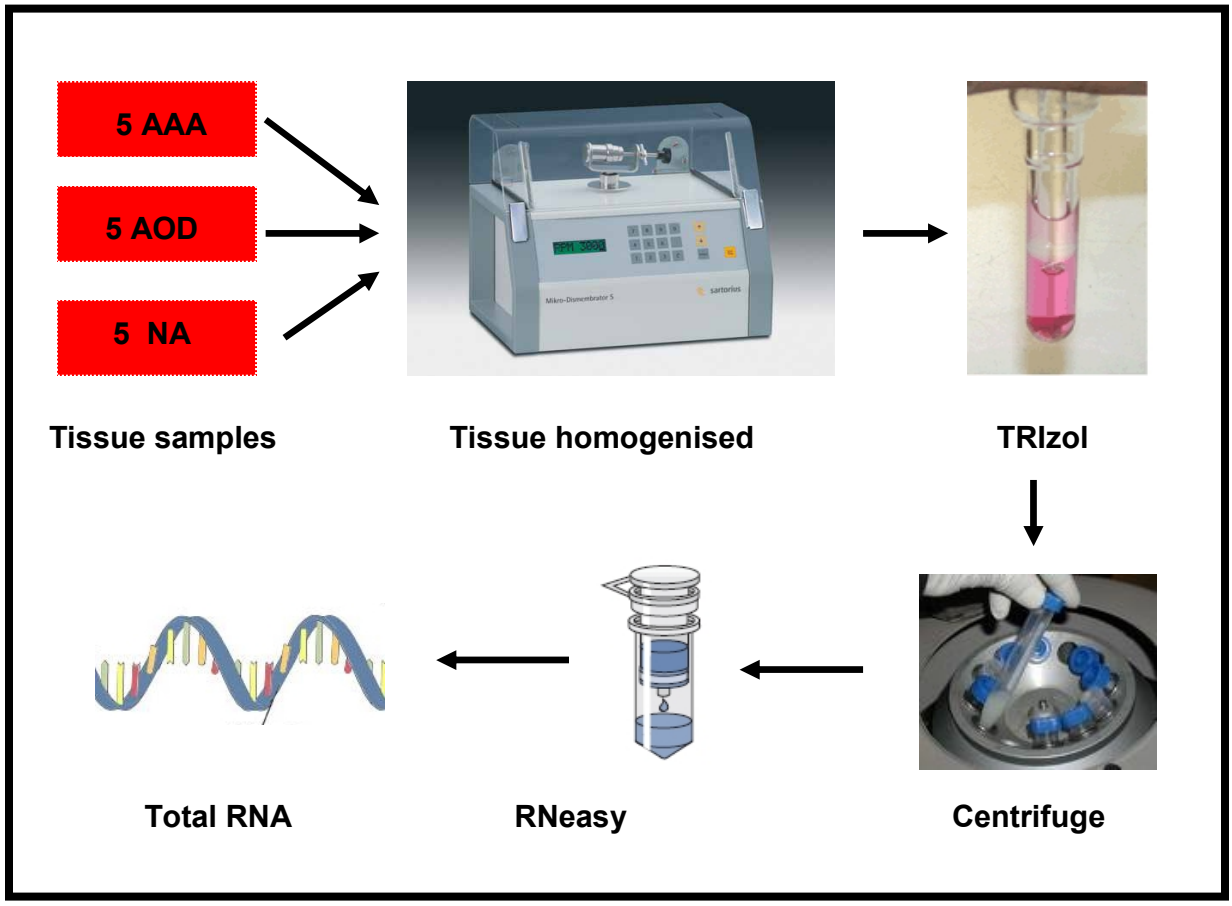


Figure 2.9 Schematic representation of RNA extraction and purification using the RNEasy midicolumn (Qiagen)

2.4 RNA quantification and quality

The quality and total concentration of total RNA in the sample was determined using the Bioanalyser 2100 and Nanodrop systems.

2.5 RESULTS

2.5.1 Comparison of two methods of RNA isolation

The purity and the integrity of the RNA were affected by both the age of the material (Figure 2.10A) and the method of RNA isolation (Figures 2.10B and C). When isoproponol was used to precipitate the RNA the purity was compromised by the presence of genomic DNA and ethanol contamination (arrow Fig 2.10B). These were absent following isolation using the Qiagen midicolumn. Archived RNA which had gone through a process of recurrent thawing and freezing underwent degradation as shown by the peak in the fast region in Figure 2.10A (arrow). None of the archived RNA samples were used in this study. All RNA samples used in this study were extracted by me using Trizol and precipitated and purified using the RNA midi column kit (Qiagen, UK) to minimise contamination with genomic DNA and organic solvents (Section 2.3.3.2).

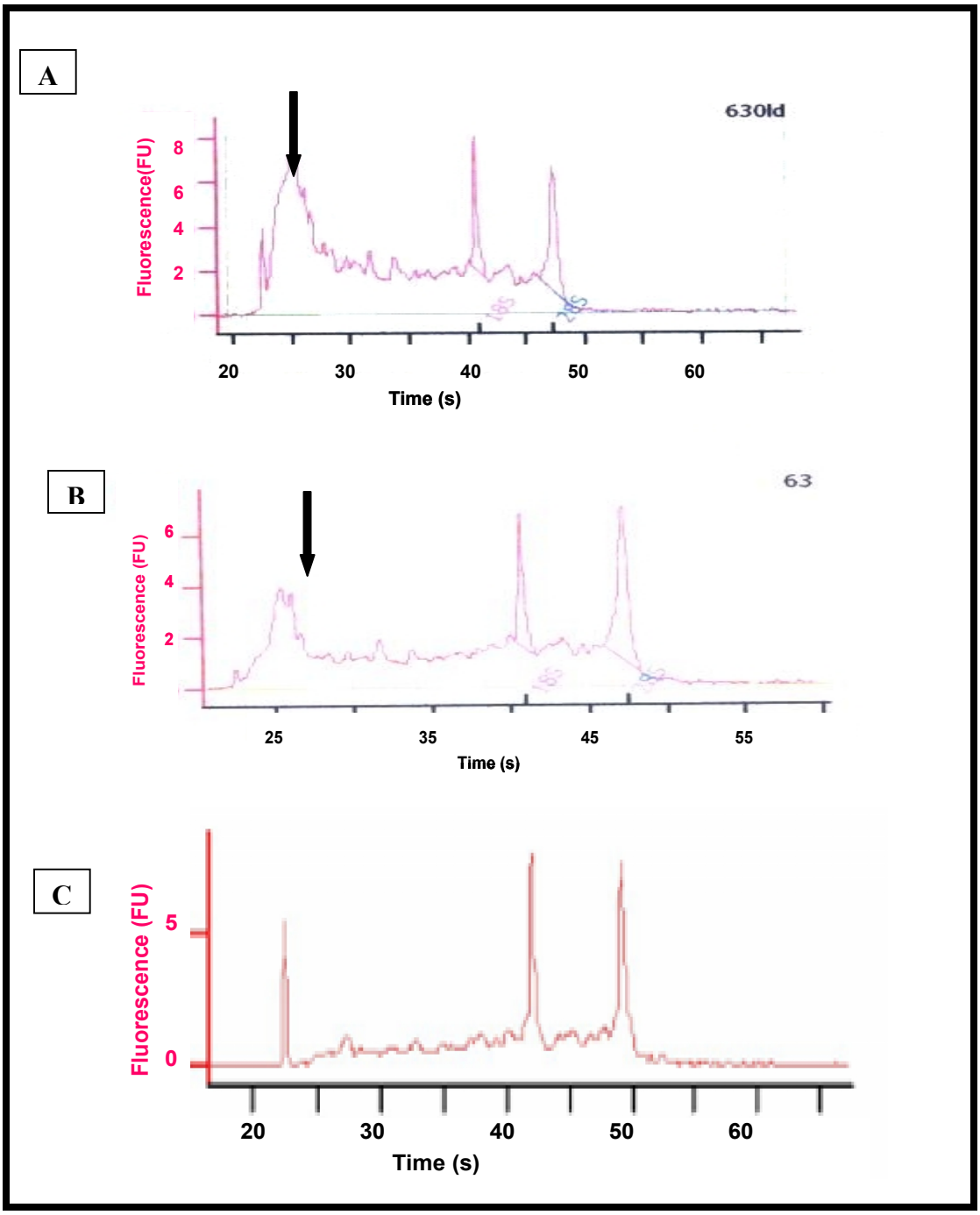


Figure 2.10 Bioanalyser traces from the same sample. (A) RNA extracted and archived for 1 year. (B) RNA extracted using Trizol and isopropanolol. (C) RNA extracted using Trizol followed by Qiagen midicolumn. The arrows indicate degraded RNA and contamination with genomic DNA or inorganic solvents.

2.5.2 Quality of all RNA samples extracted

Tables 2.1-2.3 summarise the processing time for each sample (i.e. from time of collection of the tissue sample to the extraction of RNA) and the quality of the RNA yielded. Quality of RNA extracted is inversely correlated with the processing time. Only RNA with RIN > 5.5 were used in the microarray and qRT-PCR experiments.

Table 2.1 Quality of RNA extracted in AAA group.

AAA samples	Processing time	RIN
AAA1	5 days	8.5
AAA2	10 days	7.5
AAA3	10 days	7.6
AAA4	2 months	7.3
AAA5	3 months	7.5
AAA6	3 months	7.5
AAA7	4 months	6.2
AAA8	4 months	7.1
AAA9	6 months	6.6
AAA10	3 months	6.4
AAA11	8 months	7.0
AAA12	8 months	7.1

AAA13	6 months	7.2
AAA14	9 months	6.1
AAA15	9 months	6.2
AAA17	12 months	5.3
AAA18	12 months	5.2
AAA19	12 months	6.1
AAA20	16 months	4.2
AAA21	16 months	4.5
AAA22	18 months	6.3
AAA23	16 months	4.5
AAA24	18 months	6.1
AAA25	16 months	5.1
AAA26	18 months	4.2
AAA27	18 months	5.3

Table 2.2 Quality of RNA extracted in AOD group

AOD Sample	Processing time	RIN
AOD1	4 months	6.7
AOD2	6 months	7.2
AOD3	6 months	6.8
AOD4	8 months	6.9
AOD5	6 months	6.1
AOD6	12 months	6.1
AOD7	13 months	6.2
AOD8	8 months	6.2
AOD9	12 months	5.7
AOD10	15 months	6.2
AOD11	18 months	5.3
A0D12	20 months	5.2
AOD13	22 months	5.1
AOD14	18 months	4.8
AOD15	24 months	4.8
AOD16	18 months	5.0
AOD17	22 months	5.2

Table 2.3 Quality of RNA extracted in NA group

NA samples	Processing time	RIN
NA1	6 months	6.7
NA2	8 months	7.0
NA3	6 months	6.2
NA4	8 months	6.5
NA5	8 months	6.3
NA6	9 months	6.5
NA7	12 months	6.2
NA8	13 months	6.0
NA9	12 months	4.3
NA10	14 months	3.2

2.5.3 Patient demographics for microarray study

Patient demographics for the samples used in the microarray experiment are shown in Table 2.4. Patients were age and sex matched.

Table 2.4 Demographics of patients used in microarray experiment

Demographics	AAA (n=5)	AOD (n=5)	NA (n=5)
Mean age	70 (63-77)	62 (53-73)	56 (50-62)
Sex (M/F)	5 / 0	5 / 0	5 / 0
Aortic diameter	6.6 (5.5-8.0)	-	-
Smoking	3	3	2
Hypertension	3	2	2
IHD	3	3	0
Diabetes	2	3	0

The sample size in each group was five. Though patients in the AOD group tended to be younger than in the AAA group, there was no difference in their co-morbidities. Patients from the NA cohort were younger and had significantly less co-morbidity than those in the AAA or AOD cohorts, as expected.

2.5.4 RNA profiles of aortic tissues used in the microarray experiment

Only RNAs with the highest RIN in each group were used in the microarray study. Bioanalyser traces for the RNA are shown in figures 2.11-2.13 and the RIN values are summarised in Table 2.5.

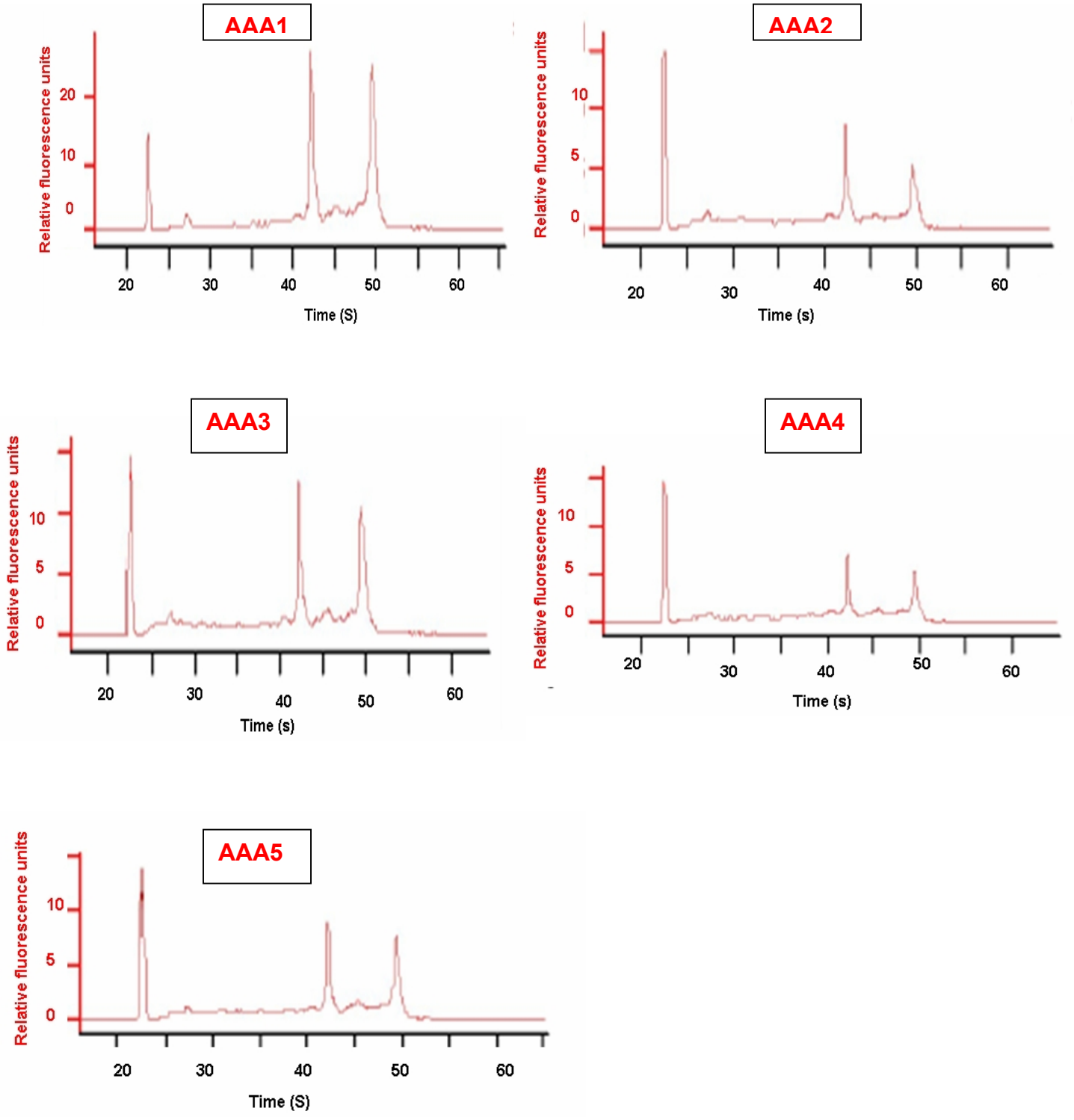


Figure 2.11 Bioanalyser traces of RNA profiles of abdominal aortic aneurysm tissues.

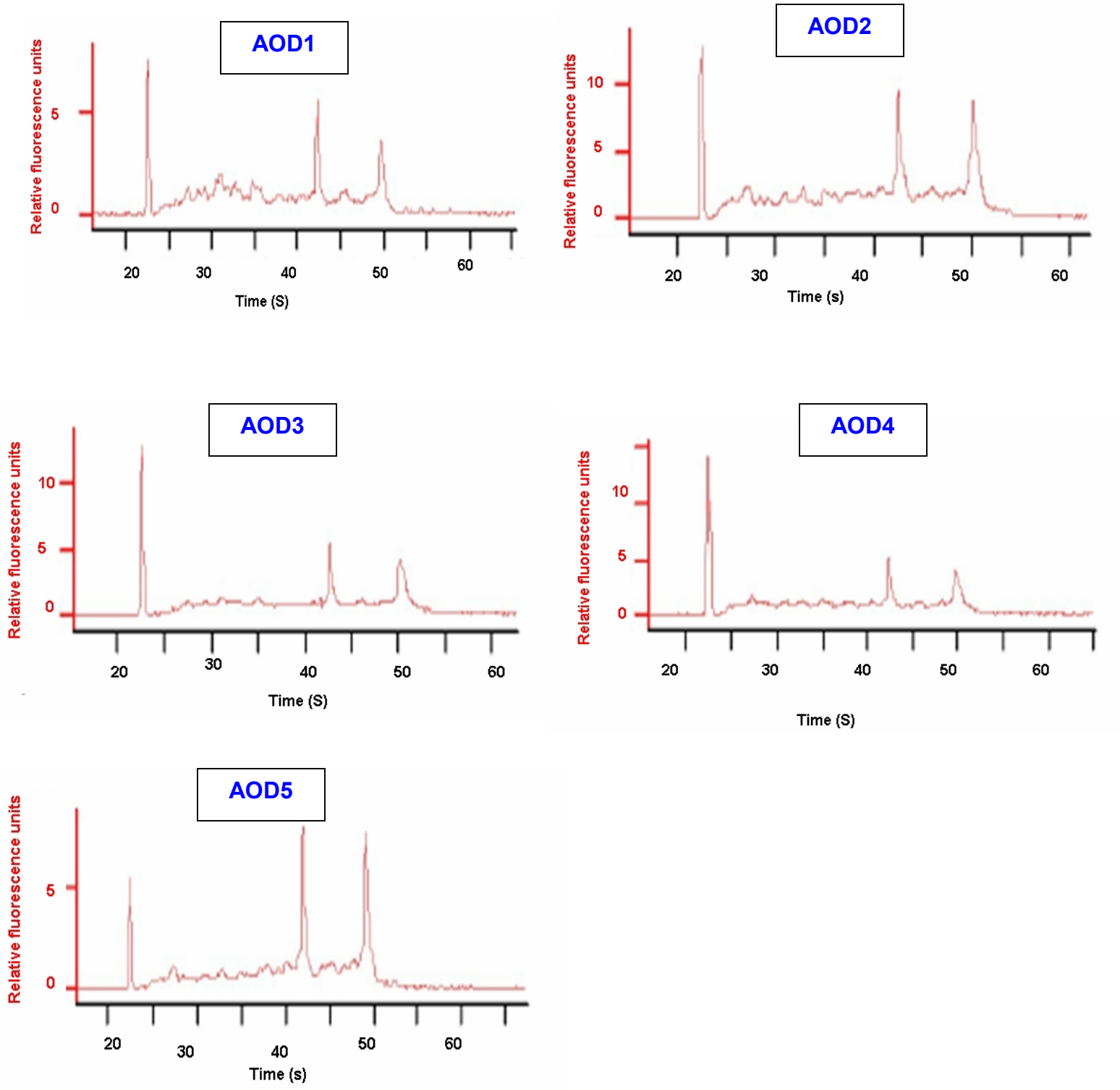


Figure 2.12 Bioanalyser traces of RNA profiles of aortic occlusive disease tissues.

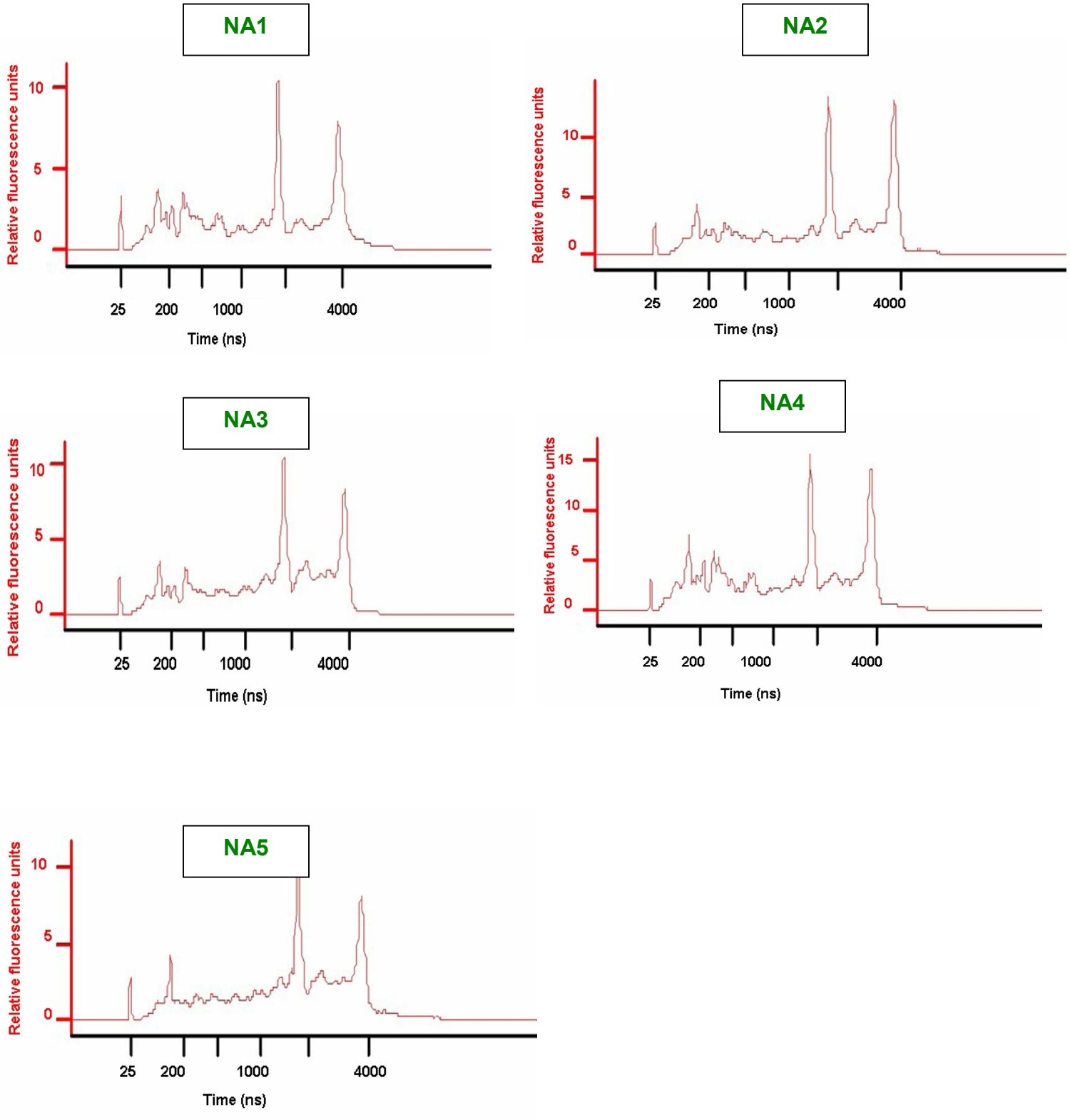


Figure 2.13 Bioanalyser traces of RNA profiles of normal aortic tissues.

Table 2.5 Summary of RNA (RIN and A260/280) ratio for all samples measured using the Bioanalyzer and Nanodrop respectively

Sample	RIN	A260/280
AAA1	8.5	2.1
AAA2	7.5	2.1
AAA3	7.6	2.1
AAA4	7.3	2.1
AAA5	7.5	2.0
AOD1	6.7	2.1
AOD2	7.2	2.1
AOD3	6.8	2.1
AOD4	6.9	2.1
AOD5	6.1	1.9
NA1	6.7	2.0
NA2	7.0	2.0
NA3	6.2	2.1
NA4	6.5	2.0
NA5	6.3	2.0

2.6 Discussion

RNA was extracted from aortic tissue using Trizol reagent however the RNEasy midi kit protocol (Qiagen) was preferred to the isopropanol technique for RNA purification. The RNEasy midi kit protocol involves a DNAse digestion step to decrease contamination with genomic DNA and the highly adsorbent column decreases the risk of contamination with organic solvent. The superiority of this technique was shown by the decreased noise in the fast region of the bioanalyser traces (Figures 10B and 10C).

RIN numbers for AAA samples were higher than those from either AOD or normal aortic wall. This could be explained by the fact that the AAA samples were stored for a shorter time prior to RNA extraction compared with AOD and NA samples. The AOD samples, available for this study, although quickly snap-frozen following collection, had been archived at -80ºC up to months before extraction. Unfortunately, open surgery for aorto-iliac bypass is rare with the advent of less invasive endovascular techniques and therefore limited the pool of AOD samples available. The results on RNA quality from AOD also confirm our experience of RNA extraction from other occluded arteries (carotid), where quality was likewise a problem even though samples were freshly extracted[258]. Normal aortic wall samples were obtained from UKHTB and according to their records had much longer processing times. This affects the quality of the RNA and is reflected by the increased noise in the fast regions and inter-regions of the bioanalyser traces. Picochips were used to analyse the RNA from normal aortic

wall samples (explaining the difference in scaling on the x-axis of the electrophoregrams between AAA and normal aortic wall or AOD and normal aortic wall) as the yield of RNA from these samples were smaller and the picochips allowed for a much smaller volume to be used for RIN analysis on the bioanalyser.

RNA quality and yield are also dependent on the disease processes affecting the tissues. This probably reflects disease-specific physiological stresses on the tissues. For example lower RIN value and yield are characteristic of some tissues such as liver or lung independent of the sources[259]. None of the microarray experiments carried out on human aortic tissues[95;135;250] have reported on the quality of the RNA used. When degraded RNA is used in a gene expression experiment, genes with high levels of expression can still be characterised with respect to relative expression levels. However, degradation compromises the ability to detect differences in expression of genes expressed at low levels[260].

All the RNA used for the micro-array experiment showed high level of expression of housekeeping genes on the microarray test chips (Affymetrix) (Section 3.4.6). This allowed us to proceed with downstream experiments with confidence in the quality of the samples.

Chapter 3

Micro-array analysis

3.1 Introduction

3.1.1 Principle of DNA microarray technology

DNA microarray technology is based on the principle of hybridisation between two DNA strands. Hybridisation is the property of complementary nucleic acid sequences to specifically pair with each other by forming hydrogen bonds between complementary nucleotide base pairs. Two DNA strands will hybridise if they are complementary to each other according to the Watson-Crick rule. The strands of DNA can be replaced by RNA and hybridisation will still occur as long as there is complementarity[261].

In a DNA microarray experiment, many genes-specific 'probes' are immobilised on a solid support (usually glass) and the array is exposed to labelled cDNA 'targets' derived from a biological sample. Both specific and non-specific bonding sequences occur due to the high number of complementary base pairs in a nucleotide sequence. The array is cleared of non-specific bonding sequences through a washing process. The labelled cDNA targets that remain bound to a probe sequence on the array generates a signal that depends on the strength of the hybridisation. The strength of the signal at a particular spot on the array depends on the amount of labelled cDNA targets that binds to a gene-specific probe present at that particular spot[262].

Microarray technology has been used mainly for gene expression analysis or for point mutation/SNP analysis. Gene expression analysis has helped in elaborating the pathogenesis of different cancers, namely hepatocellular carcinoma[263;264], Hodgkin's lymphoma[265], breast cancer[266] and colorectal cancer[267]. Gene expression analysis has also played an important role in drug discovery, metabolism and toxicity[268;269], microbiological and infectious disease[270;271], genotyping[272;273] and disease diagnostics[274;275].

3.1.2 Fabrication of DNA microarray

DNA microarrays are generally fabricated on glass, silicon or plastic substrates. Different probes are attached within micrometers of each other so that a DNA microarray may have up to 10^6 test sites in a 1-2 cm^2 area. The probes can include synthetic oligonucleotides or larger DNA/RNA fragments. A variety of techniques are used to spot the probes onto the test sites[276]. These are discussed below.

3.1.2.1 Photolithographic process (Affymetrix).

Affymetrix microarrays are manufactured using a combination of DNA synthesis chemistry and photolithography techniques. A glass array is first coated with a chemical linker containing photolabile protecting groups. A mask is applied exposing selected portions of the probe array to ultraviolet light. Illumination removes the photolabile protecting groups enabling selective nucleoside

phosphoramidite addition only at previously exposed sites. A different mask is then applied and the cycle of illumination and chemical coupling is performed again. By repeating this cycle, a specific set of oligonucleotide probes is synthesized with each probe type in a known location. The completed probe arrays are then packaged into cartridges (Figure 3.1)[276].

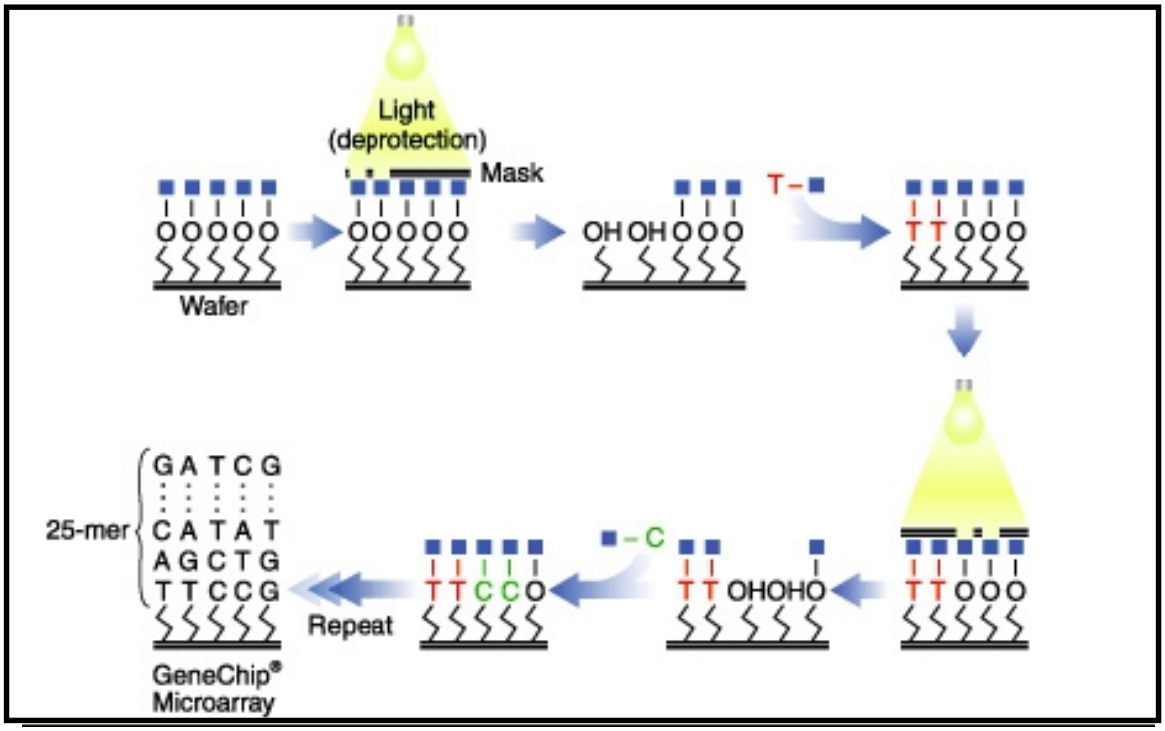


Figure 3.1 Photolithography and combinatorial chemistry technology for manufacturing Affymetrix Gene Chip[276].

3.1.2.2 Spotted arrays

A robot spotter is used to move small quantities of probe in solution from a microtitre plate to the surface of a glass plate[277]. The probe consists of an

oligonucleotide that is complementary to a unique gene. The glass slides are first coated with a polylysine reagent, a highly positively charged compound that improves adherence of oligonucleotides and a robot is used to spot probes onto the glass slides. Subsequent preparation and hybridisation to the array is similar to the Affymetrix protocol discussed below (Section 3.1.3)[276].

The main advantage compared with the Affymetrix array is that any probe can be designed for spotting onto the array. The disadvantages are that spotting will not be as uniform as in situ synthesised Affymetrix chips and the cost of designing the probes are high.

3.1.2.3 Digital Micromirror arrays (Geniom One, NimbleGen).

This technique uses a digital micromirror device in combination with a mercury lamp to control light-directed synthesis of oligonucleotide arrays. The process involves deprotection of photolabile groups and coupling with DNA building blocks. Repeated cycles of photodeprotection and coupling result in oligonucleotide chain elongation with a specific sequence for each spot[278].

3.1.2.4 Inkjet arrays (Agilent).

Printing technology developed for inkjet printer is used. Pre-synthesized oligonucleotides are printed directly onto the glass surface. These are known as deposition arrays[279].

3.1.2.5 Bead arrays (Illumina).

Bead array technology is based on 3-micron silica beads that self assemble in microwells on a substrate which is either fibre optic bundles or planar silica. When randomly assembled on one of these two substrates, the beads have a uniform spacing of about 5 microns. Each bead is then covered with hundreds of thousands of copies of a specific oligonucleotide[280].

3.1.3 General overview of target preparation and hybridisation

The primer consisting of a T7 oligo (dT) is added to the total RNA sample. The primer binds mRNA only, as it has a polyA tail (selective binding of adenine on mRNA and thymine on primer) and a reverse transcriptase starts synthesis of the first strand of cDNA from the mRNA. An RNA degrading enzyme (RNAseH) removes the primer and allows the binding of DNA polymerase I which starts the synthesis of the second strand of cDNA. Ligase enzyme catalyses formation of phosphodiester bonds between the strands of cDNA forming double stranded DNA. The cDNA is then reverse transcribed to cRNA which is labelled with biotin. The biotin-labelled cRNA is then fragmented into smaller oligonucleotides of about 25 basepairs. The fragmented oligonucleotides are then hybridised with the oligonucleotides on the genechip. The genechip is stained with streptavidin-phycoerythrin which binds to biotin and fluoresces under the laser in the scanner. The intensity of the fluorescence reflects the level of expression of the gene (Figure 3.2)[276].

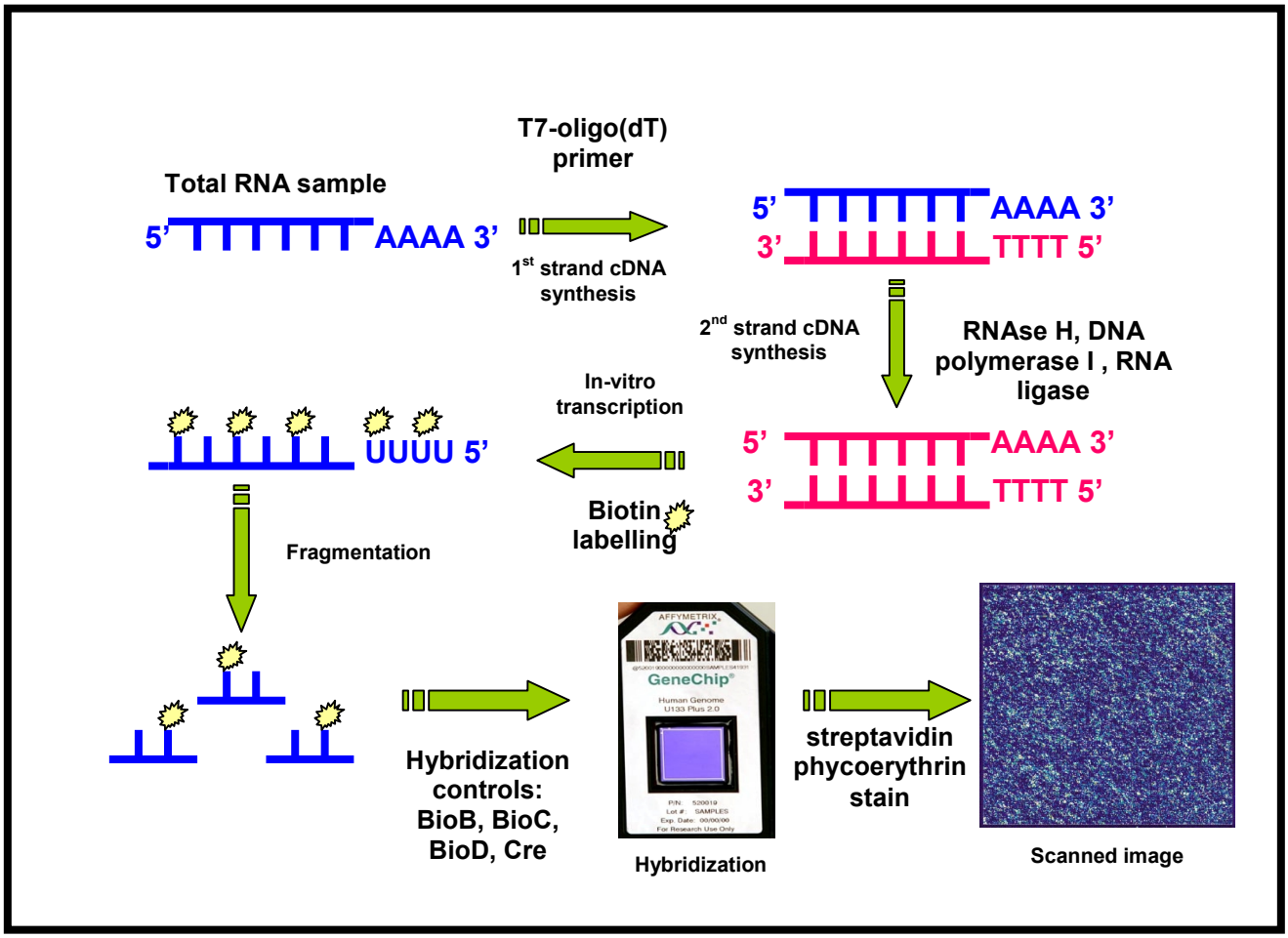


Figure 3.2 Overview of different steps in the micro-array process

3.2 Methods

3.2.1 Target preparation

The one-cycle cDNA synthesis kit (Affymetrix) was used for steps (i) and (ii) (Appendix A).

(i) First strand cDNA synthesis. Total RNA (5µg) from each sample was placed in a 0.2mL RNAse free PCR tube (Eppendorf, UK). The volume of the sample was reduced to less than 10µl using a Gyrovap vacuum system at 1500g and 20ºC. T7-Oligo (dT) primer (2µl of 50µM) was added and the solution made up to 12µl with RNase-free water. The contents of the tube were mixed by flicking and the reaction mix incubated for 10 minutes at 70ºC. The sample was cooled to 4ºC for at least 2 minutes.

A first strand master mix (FSMM) was prepared using 4µl of 5×concentration of first strand reaction mix, 2µl of 0.1M dithiothreitol (DTT) and 1µl of 10mM of deoxyribonucleotide triphosphate (dNTP). The FSMM (7µl) was added to each RNA/T7-Oligo (dT) primer mix above to give a final volume of 19µl. The reaction mix was incubated at 42ºC for 2 minutes. SuperScript II (reverse transcriptase) (1µl) was added for a final volume of 20µl. The reaction was incubated at 42ºC for 1 hour and cooled to 4ºC for at least 2 minutes.

(ii) Second strand cDNA synthesis. Second strand mastermix (SSM) was prepared using the following reagents in the proportion shown in Table 3.1.

Table 3.1 Reagents used for synthesis of 2nd strand of cDNA.

Component	Volume (µL)
RNase-free water	91
5 × 2nd Strand Reaction Mix	30
dNTP , 10mM	3
E. coli DNA ligase	1
E. coli DNA polymerase I	4
RNase H	1
Total Volume	**130**

The SSM (130µL) was added to each first strand synthesis sample from step (i) for a total volume of 150µL. The reaction was incubated for 2 hours at 16ºC. T4 DNA polymerase (2µL) was added to each sample and incubated at 16ºC for 5 minutes, after which 10µL of EDTA was added to stop the reaction.

(iii) Clean-up of the double-stranded cDNA. The sample clean up module kit (Affymetrix) was used. cDNA binding buffer (600µL) was added to the double-

stranded cDNA synthesis preparation from step (ii). The mixture was added to the cDNA cleanup spin column and centrifuged for 1 minute at 3000rpm. The non-adsorbed sample was discarded. cDNA wash buffer was pipetted onto the spin column and centrifuged for 1 minute at 3000rpm. The column was dried by centrifuging at 4000rpm for 5 minutes. cDNA elution buffer was pipetted directly on the spin column and eluted by centrifuging at 4000rpm for 1 minute.

(iv) Synthesis of biotin-labelled cRNA. The GeneChip in vitro transcription (IVT) labelleling kit (Affymetrix) was used. The template cDNA synthesized above was added to the reagents in Table 3.2. The mixture was then incubated at 37ºC.

Table 3.2 Reagents for preparation of cDNA template.

Component	**Volume (µL)**
Template cDNA	12
RNase-free water	8
10 × IVT Labelling Buffer	4
IVT Labelling NTP Mix	12
IVT Labelling Enzyme Mix	4
Total Volume	**40**

(v) Cleanup of biotin-labelled cRNA. The sample clean-up module kit (Affymetrix) was used. RNase-free water (60μL) was added to the IVT reaction and mixed. IVT cRNA binding buffer (350μL) was added to the sample and mixed. This was followed by addition of 250μL of ethanol (96-100%, molecular grade, Sigma). The sample was then applied to the IVT cRNA cleanup spin column and centrifuged for 15 seconds at 3000rpm. IVT cRNA wash buffer (500μL) was then pipetted onto the spin column and centrifuged at 3000rpm. Ethanol (500μL of 80%) was added and the spin column centrifuged at 3000rpm. The column was then dried by centrifuging it for 5 minutes at 4000rpm. The biotin-labelled cRNA was eluted with 21μL of RNAse-free water.

(vi) Quantification of the cRNA. The amount of cRNA was quantified using both the Nanodrop and Bioanalyser 2100 (Agilent). Figure 3.3 shows an example of a typical electrophoregram of cRNA from the Bioanalyser 2100. Successful cRNA synthesis is shown by a broad hump.

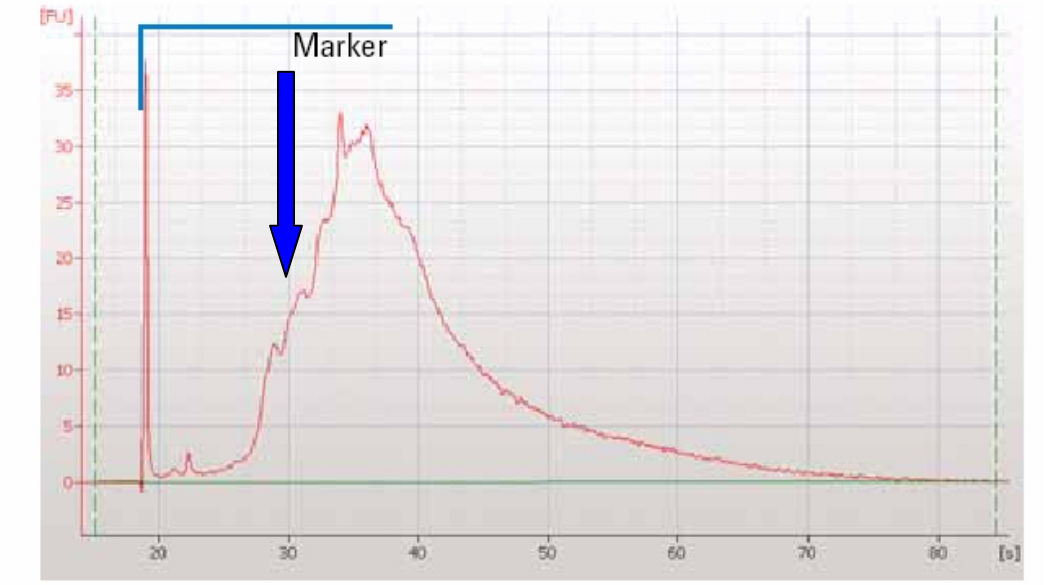


Figure 3.3 Electrophoregram of biotin-labelled cRNA. Successful cRNA synthesis is shown by a broad hump (blue arrow).

(vii) cRNA fragmentation. The sample cleanup module kit (Affymetrix) was used. The cRNA was fragmented by adding 8μL of a 5×concentrate of fragmentation buffer to each sample and the volume made up to 40μL by adding RNAse free water. The reaction was incubated at 94ºC for 5 minutes. Successful fragmentation was checked by running each sample on the Bioanalyser 2100 (Figure 3.4).

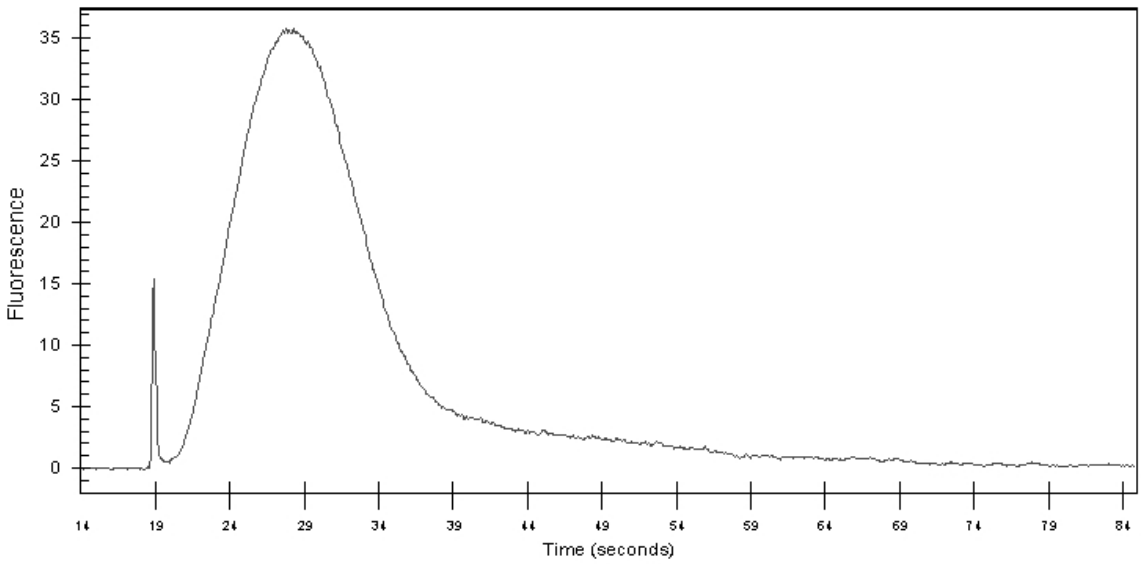


Figure 3.4 Example of an electrophoregram of fragmented cRNA. The peak will show a shift towards the left.

The Genechip hybridisation, wash and stain kit (Affymetrix) was used for steps (viii) and (ix) (Appendix A).

(viii) Target Hybridisation. A hybridisation cocktail was prepared using the reagents shown in Table 3.3. This cocktail (300µl) was added to 15µg of each cRNA sample into a 0.2mL pcr tube (Eppendorf, UK). The mixture was then heated at 99ºC for 5 minutes.

Table 3.3 Hybridisation cocktail.

Component	**Volume (µL)**
Control Oligonucleotide B2 (3nM)	5
20 × Eukaryotic Hybridisation controls	15
Herring Sperm DNA (10mg/mL)	3
BSA (50mg/mL)	3
2 × Hybridisation buffer	150
DMSO	30
RNAse free water	Variable
Final Volume	**300**

The Human genome 133 Plus 2.0 genechip was used. The genechip contains 54,675 transcripts. The probe arrays (Figure 3.5) were equilibrated to room temperature and filled with 250µL of 1×hybridisation buffer (Affymetrix). They

were incubated for 10 minutes in the hybridisation oven (Figure 3.6) at 45ºC with rotation. The hybridisation buffer was removed and the probe arrays filled with 200µL of the hybridisation cocktail before hybridisation for 16 hours at 45ºC with rotation of 100rpm.

Figure 3.5 Human genome U133 Plus 2.0 probe array (Affymetrix).

Figure 3.6 Genechip hybridisation oven (Affymetrix).

(ix) Probe array washing and staining. Immediately following hybridisation, the probe arrays underwent an automated washing and staining protocol on the fluidics station (Figure 3.7 Affymetrix). Staining and antibody mix were prepared using reagents in Tables 3.4 and 3.5 respectively and loaded on the fluidics station.

Figure 3.7 Fluidics station (Affymetrix) [276].

Table 3.4 SAPE solution mix.

Components	Volume (µL)
2 × Stain Buffer	600
50mg/mL BSA	48
1mg/mL Streptavidin Phycoerythrin (SAPE)	12
DI water	540
Total Volume	**1200**

Table 3.5 Antibody solution mix.

Components	Volume (µL)
2 × Stain Buffer	300
50mg/mL BSA	24
10mg/mL Goat IgG Stock	6
0.5mg/mL biotinylated antibody	3.6
DI water	266.4
Total Volume	**600**

The fluidics station was used to wash and stain the probe arrays. Once the fluidics station protocol was complete, the probe arrays were then ready for scanning.

(x) Probe Array Scan. The probe arrays were scanned on the Genechip Scanner 3000 (Affymetrix). The Gene-Chip Command Console (GCOS) software (Affymetrix) defined the probe cells and computes intensity for each cell.

3.3 Data output quality control.[276]

3.3.1 Probe array image inspection

The probe array image for each sample was visually inspected for artifacts (spots, scratches or array defects) that would present as a distinct pattern of abnormal intensities on the image.

3.3.2 B2 Oligo performance

B2 oligo is spiked into each sample and is used as a control for features around the edge of the chip. After scanning of the chip, the software created a grid over the image to demarcate each probe cell. Hybridisation of B2 oligo was used as a control for proper alignment of the grid for further data analysis. In order to ensure the array was working optimally, the presence of the following was assessed:

- An alternating pattern of intensities on the border (Figure 3.8).
- A checkerboard pattern at each corner (Figure 3.8).
- The array name located in the upper-left or upper-middle of each array (Figure 3.9).

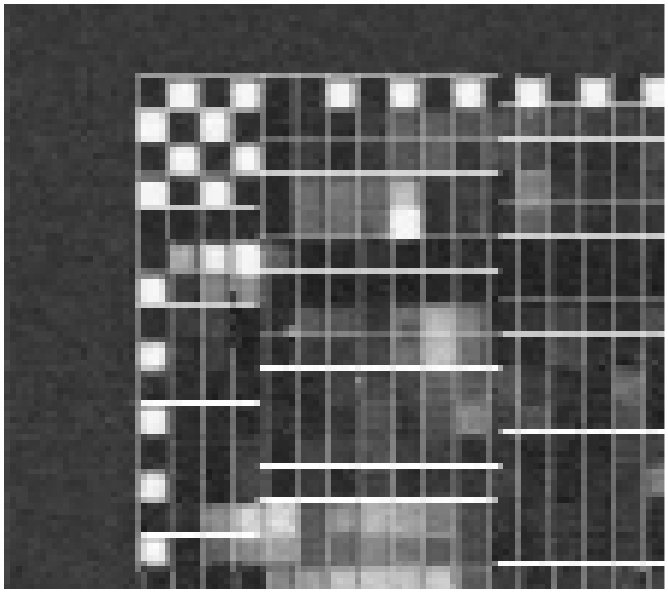


Figure 3.8 Alternating pattern of intensities at the border and checkerboard appearance at corner secondary to B2 oligo hybridisation[276].

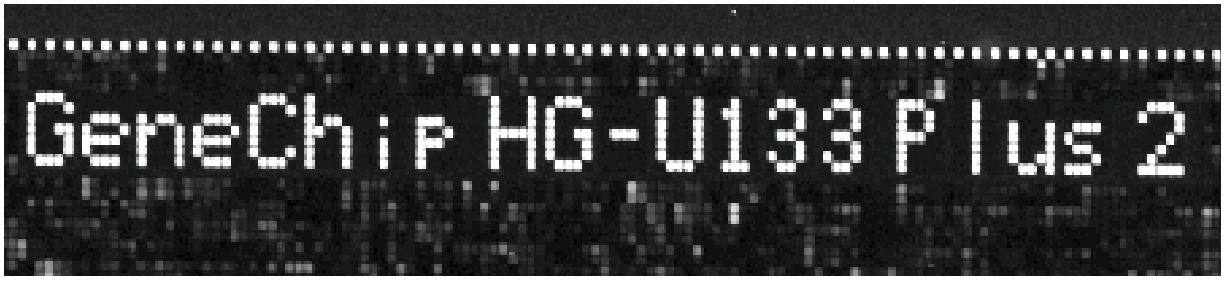


Figure 3.9 Array name showing successful hybridisation of B2 oligo[276].

3.3.3 Average background

The background value is a measure of the signal intensity caused by auto-fluorescence from the array surface as well as non-specific binding of target or stain molecules (SAPE). The background value of each genechip should ideally be between 20 and 100. The background value for each genechip is generated automatically during scanning. Replicates should ideally have comparable background values.

3.3.4 Noise

Noise is a measure of pixel-to-pixel variation on the genechip and is determined by the electrical noise of the scanner and the quality of the sample being scanned. Noise values should be comparable as the same scanner was used for all the samples.

3.3.5 Hybridisation controls: bioB, bioC, bioD and Cre

BioB, bioC and bioD are genes in the biotin synthesis pathway of E.coli and Cre is the recombinase gene from B1 bacteriophage. Oligonucleotide fragments are provided in the Affymetrix kit as a mixture of biotin labelled cRNA transcripts in staggered concentrations (1.5pM, 5pM, 25pM and 100pM final concentrations for bioB, bioC, bioD and Cre respectively). 1ml of the mixture was spiked into each sample before the hybridisation step to evaluate its efficiency (Table 3.3 – 20× Eukaryotic hybridisation controls). BioB is at the level of assay sensitivity

(1:100,000) and should be detected in at least 50% of the samples. BioC, bioD and Cre should always be detected with increasing signal values reflecting the staggering concentrations.

3.3.6 Internal control genes

Probes for the housekeeping genes, β-actin and GAPDH were used to assess RNA and assay quality. Specifically, the signal values of the 3' probe sets for β-actin and GAPDH were compared to the signal values of the 5' probe sets. The ratio of the 3' probe set to the 5' probe set should be < 3. A higher ratio indicated degraded RNA or inefficient transcription.

3.3.7 Percent present

The percentage of probes called 'Present' or expressed should be comparable between replicates. The values depend on tissue type, biological variables, array used and disease investigated.

3.3.8 Scaling factor

All arrays are scaled to a target intensity of 100 in order to correct for differences in intensity between arrays. These differences are caused by pipetting error and hybridisation, washing and staining efficiencies which are independent of

transcript expression. The scaling factors between replicates should be within 3-fold of each other.

3.4 Results

3.4.1 cRNA synthesis

Adequate cRNAs were synthesized for all the samples as shown in the bioanalyser traces in Figures 3.10A-C.

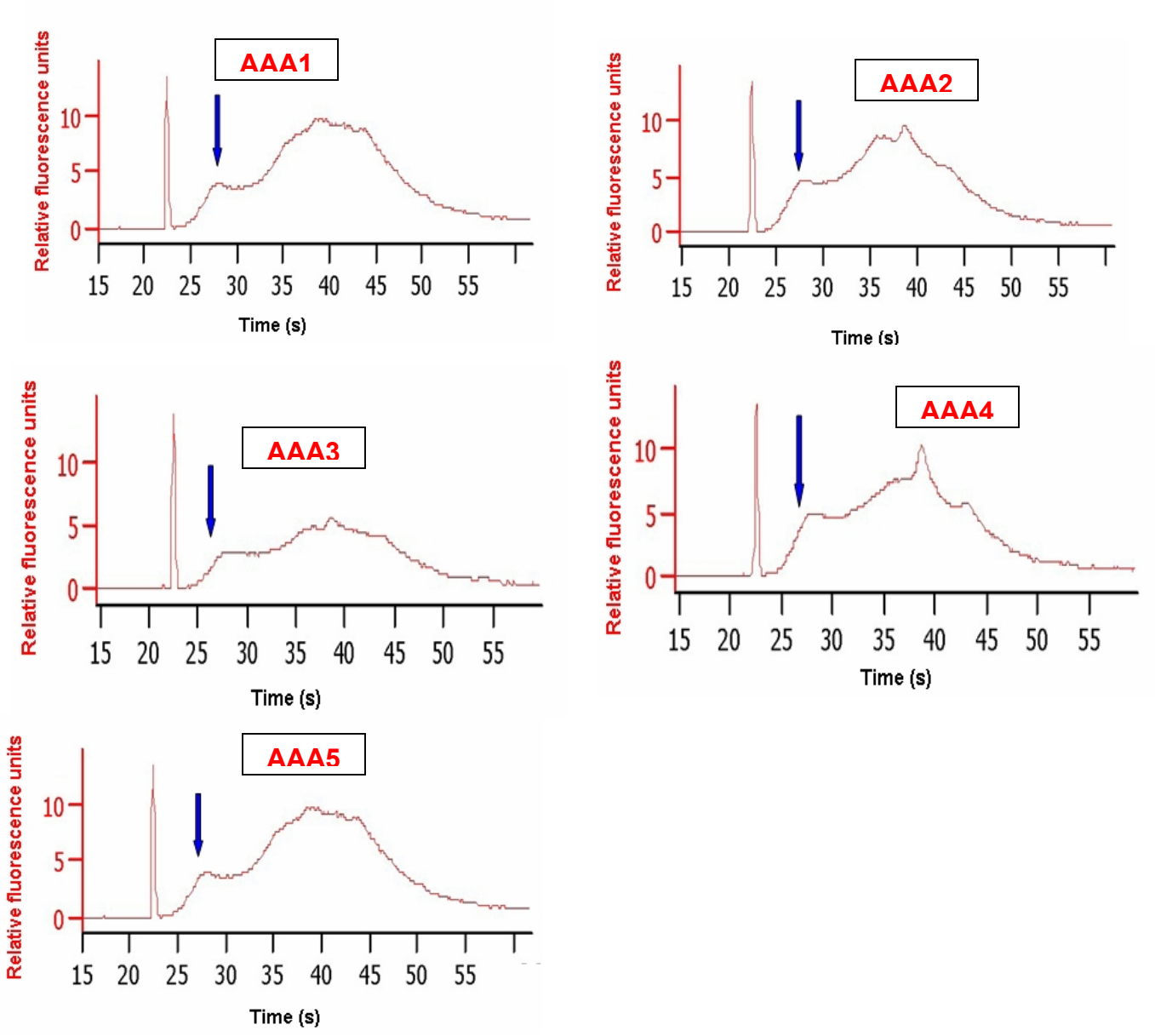
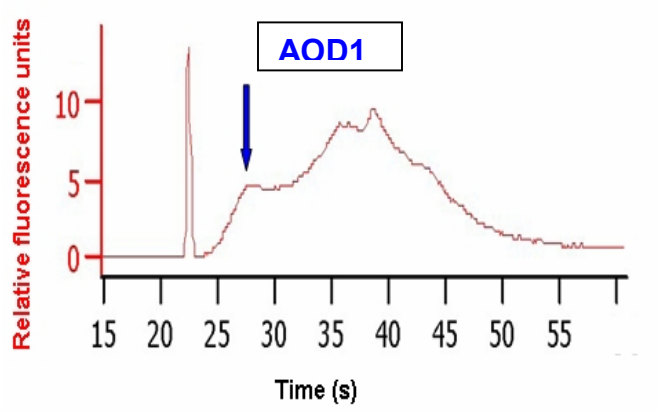
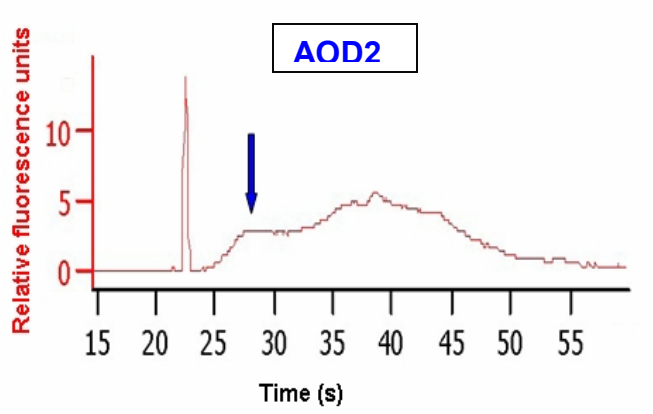
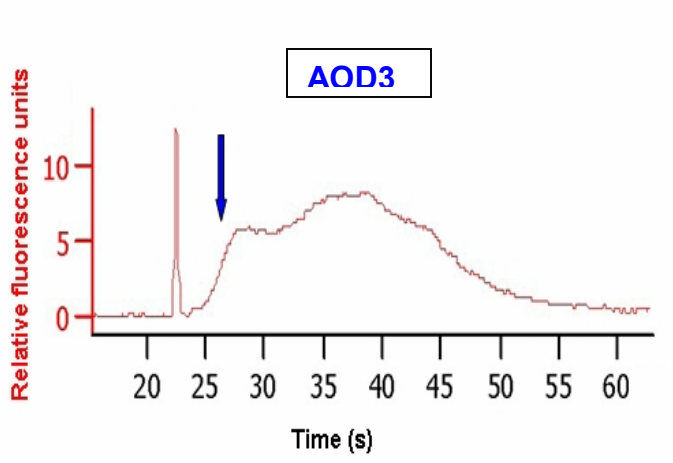
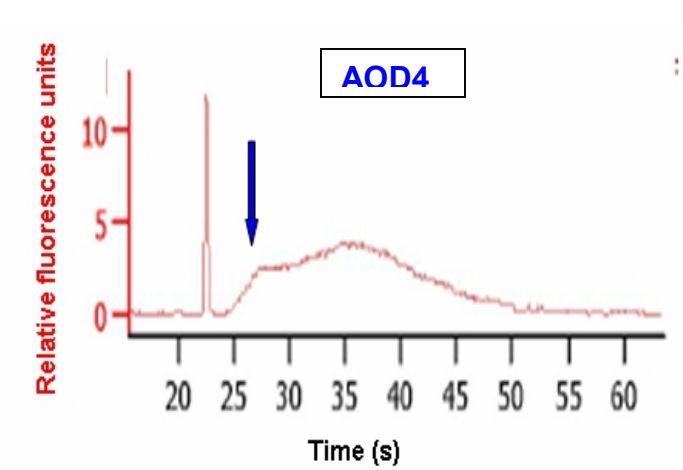


Figure 3.10A Bioanalyser traces of cRNA (blue arrow) synthesis for AAA samples.









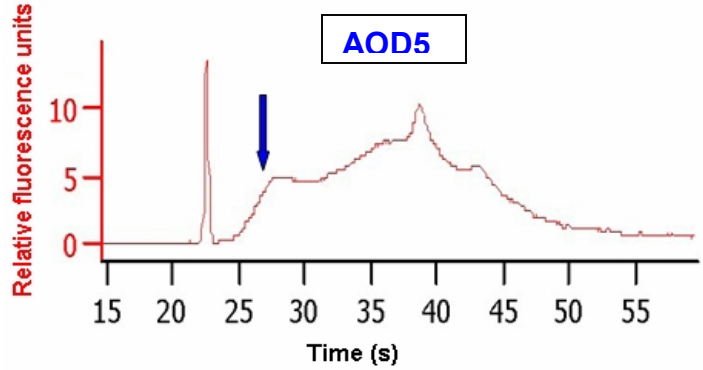


Figure 3.10B Bioanalyser traces of cRNA (blue arrow) synthesis for AOD samples.

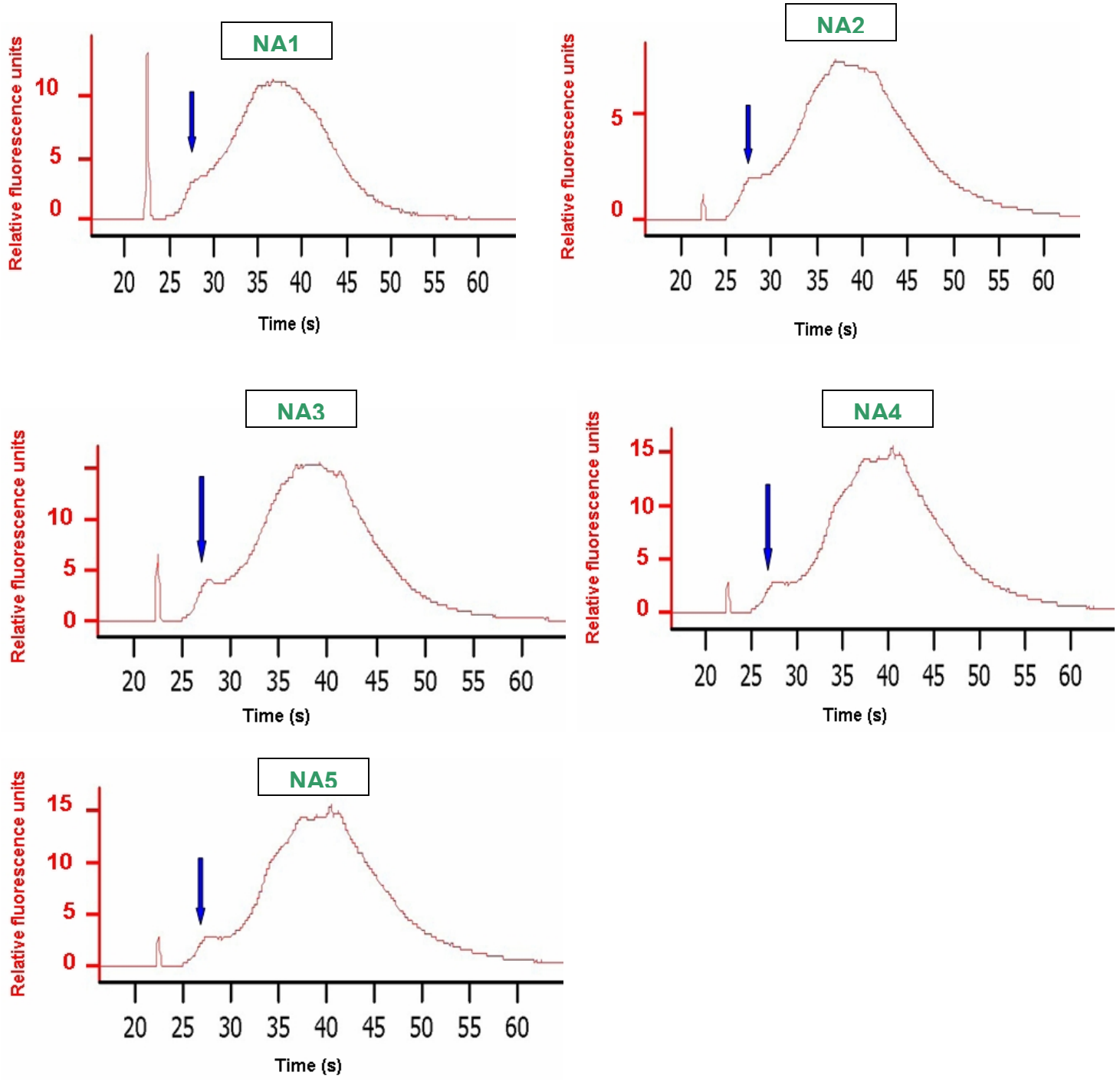


Figure 3.10C Bioanalyser traces of cRNA (blue arrow) synthesis for NA samples.

3.4.2 Fragmented cRNA

The cRNAs were then fragmented into smaller oligonucleotides of 25-200 basepairs, indicated by a left shift of the bioanalyser traces (Figures 3.11A-C). This allowed for complementary hybridisation of the cRNA to the oligonucleotides on the genechip.

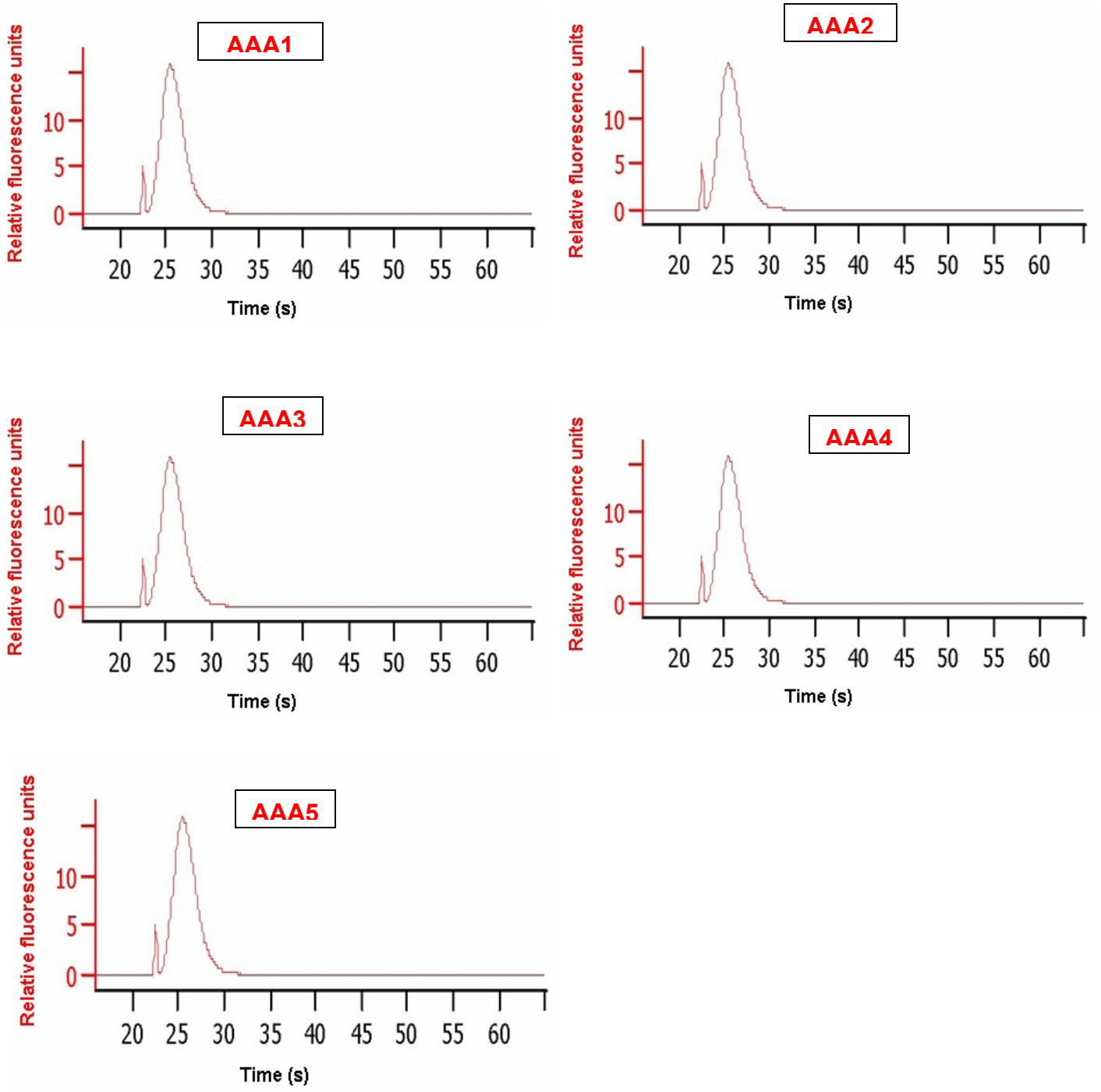


Figure 3.11A Bioanalyser traces of fragmented cRNA for AAA samples.

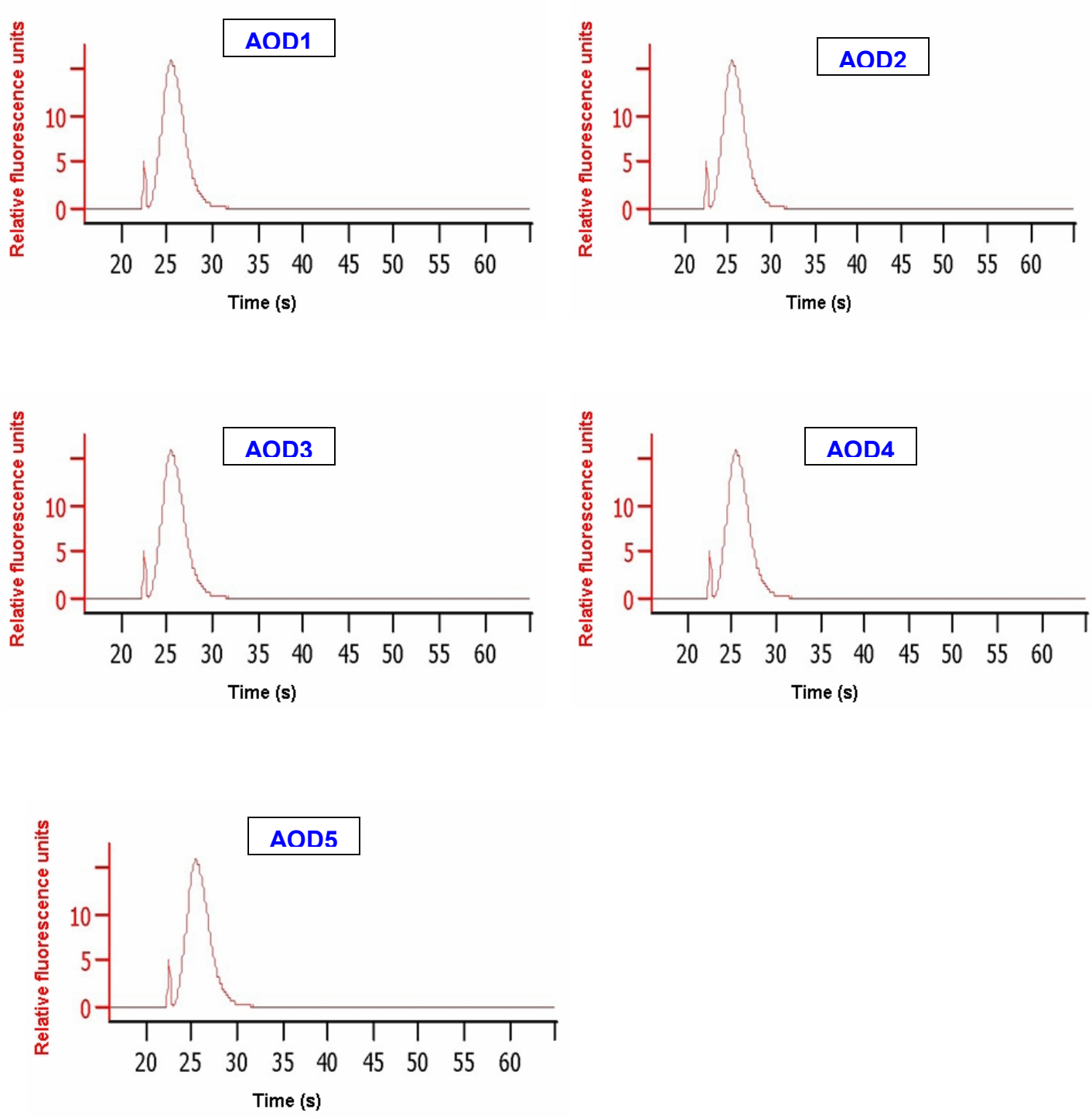


Figure 3.11B Bioanalyser traces of fragmented cRNA for AOD samples.

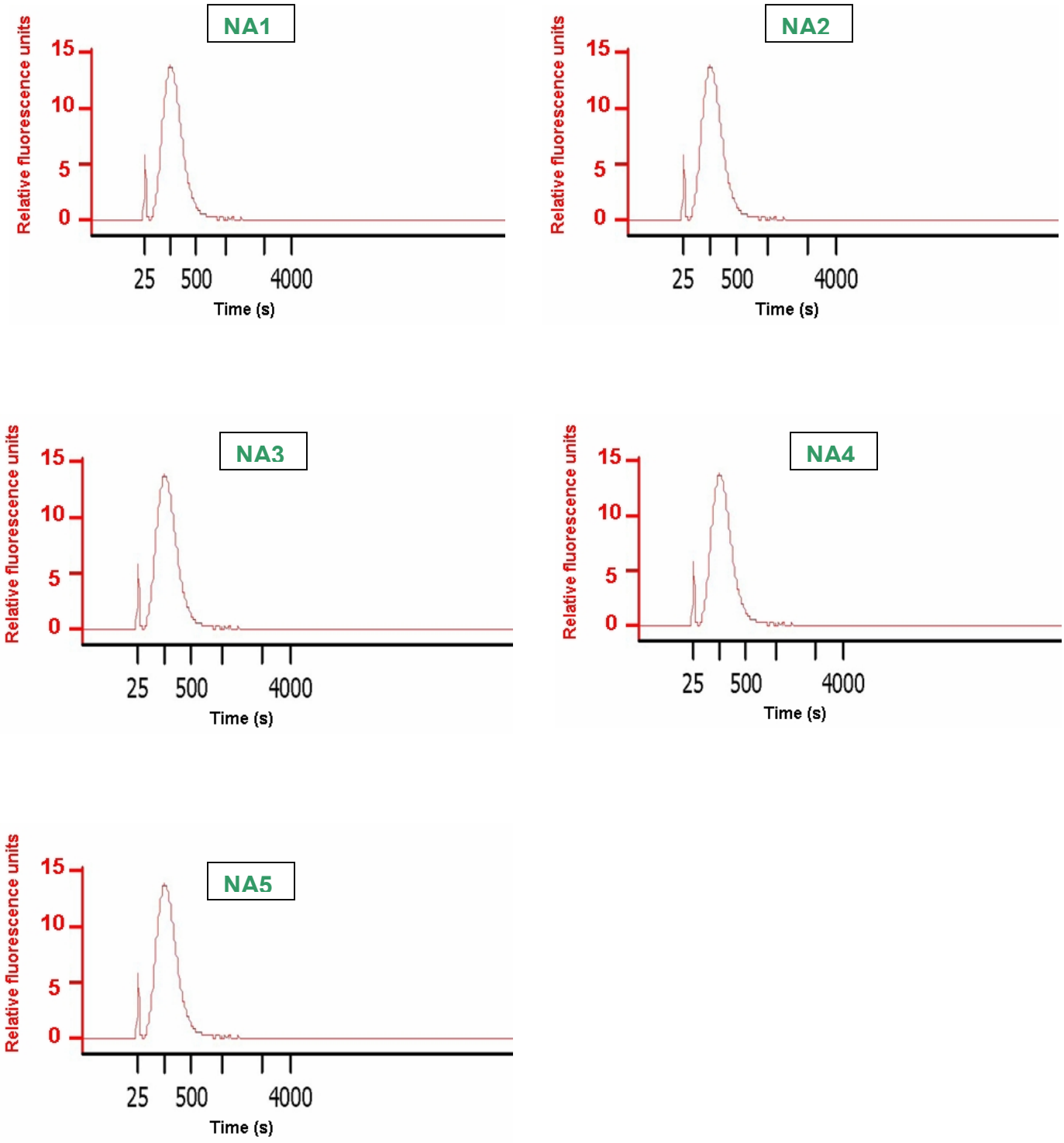
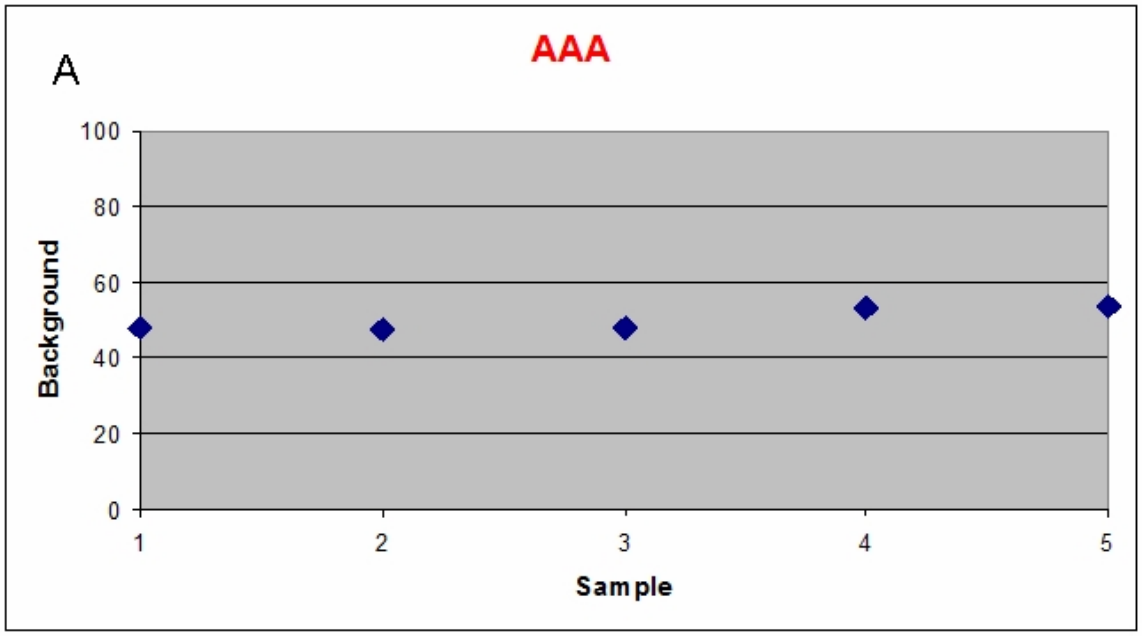
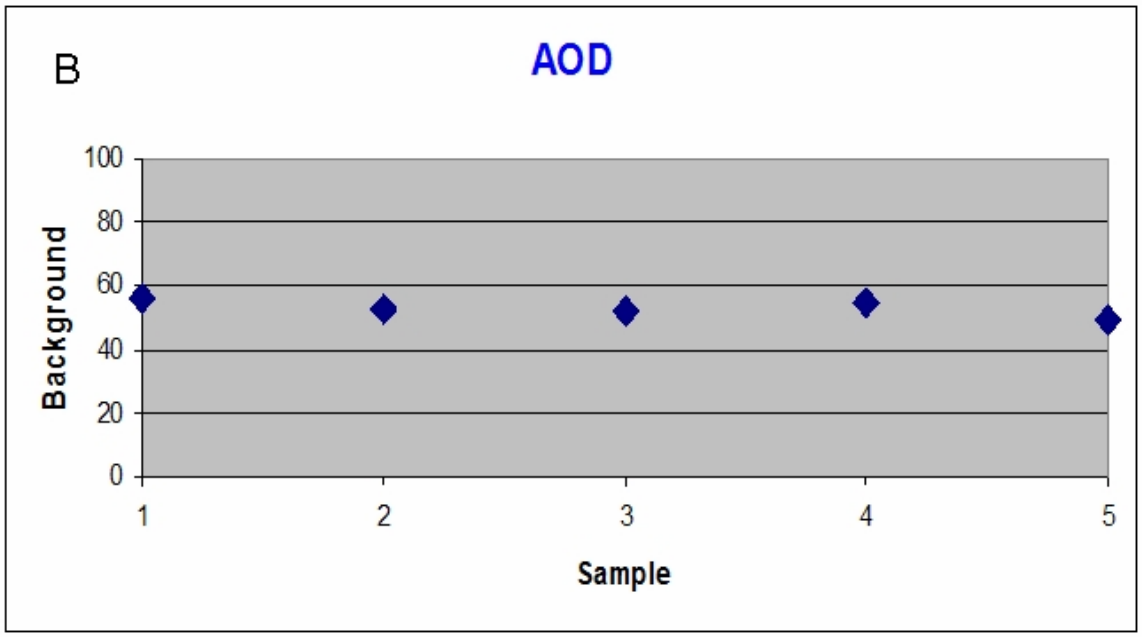


Figure 3.11C Bioanalyser traces of fragmented cRNA for NA samples.

3.4.3 Background

The background values for all the samples were within range (20-100 units) as shown in Figures 3.12 A, B and C. There was little variation between samples.





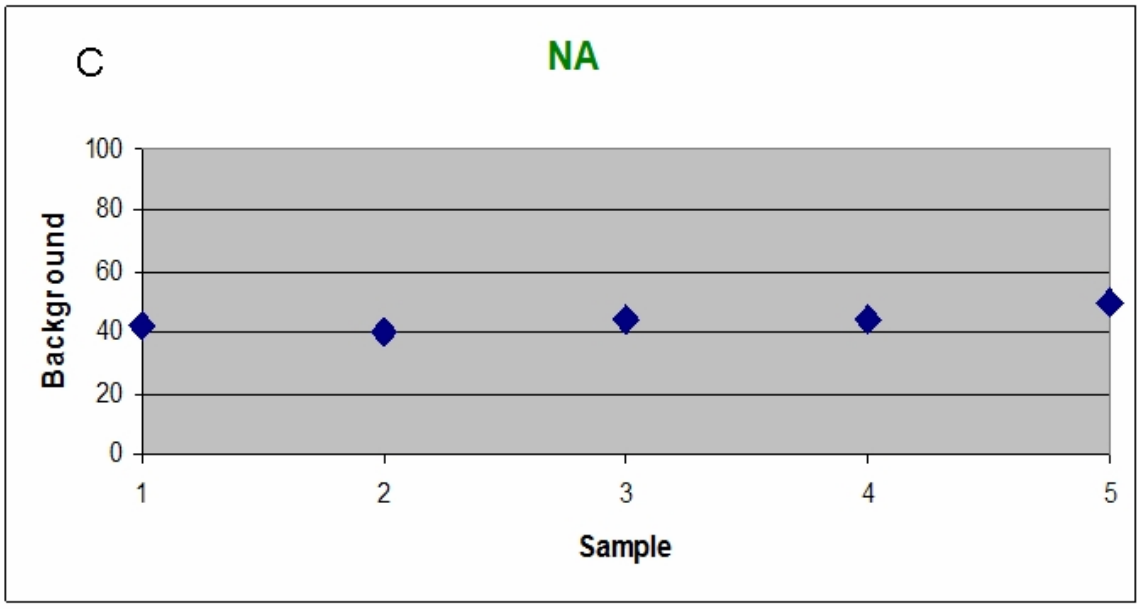
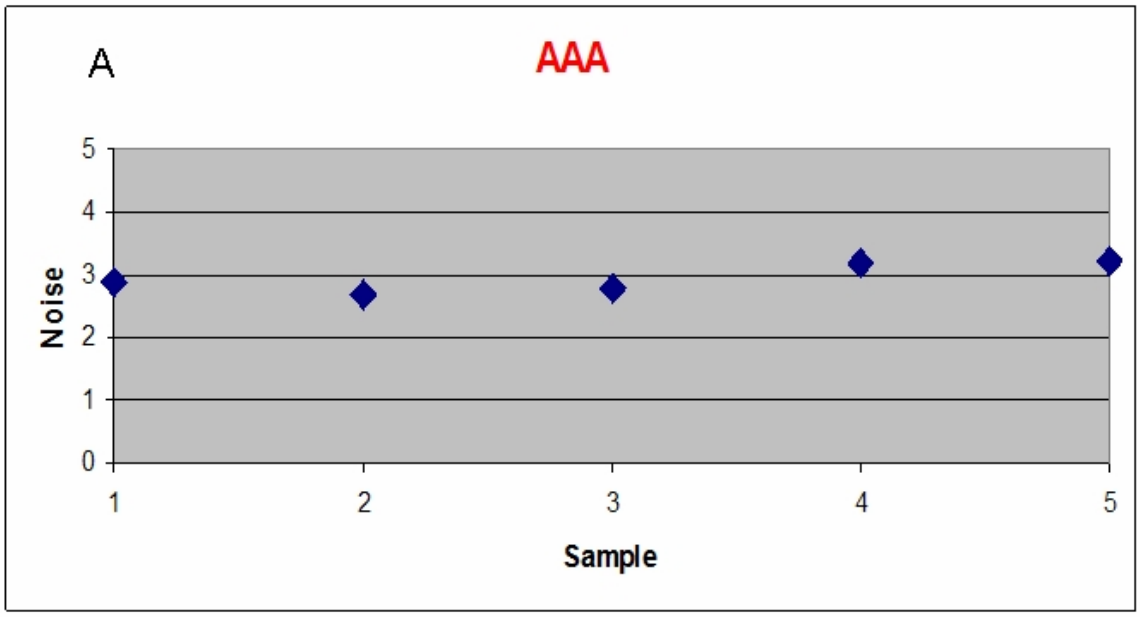
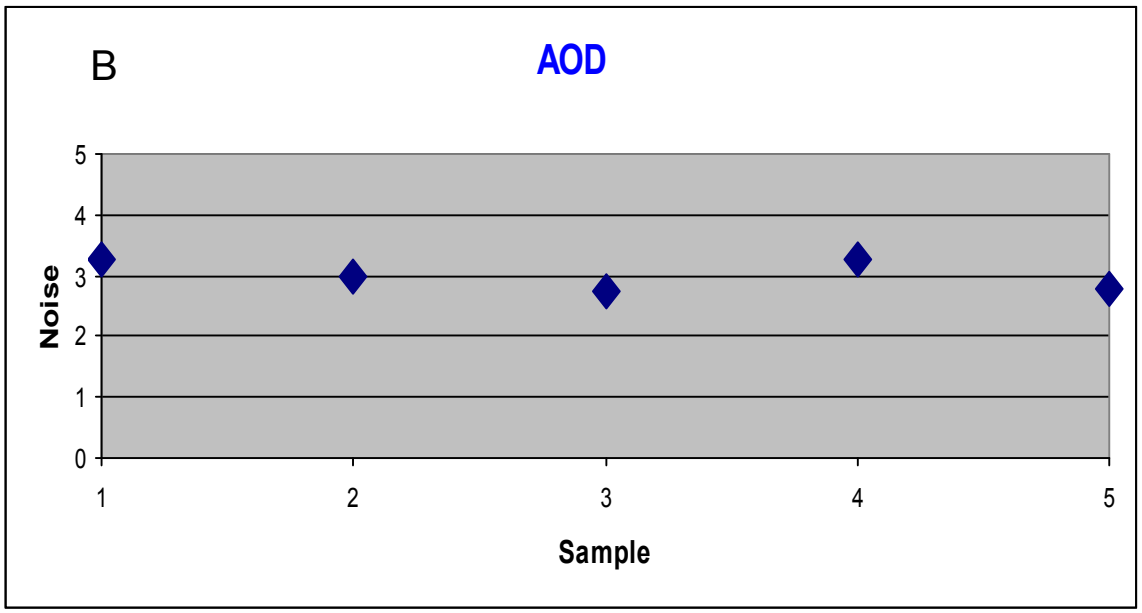


Figure 3.12 Background autofluorescence values for hybridisation of samples for A) AAA, B) AOD and C) Normal artery.

3.4.4 Noise

Noise values for all replicates within each group were between 2 and 3 units with little variation between the samples as shown in Figures 3.13 A, B and C.





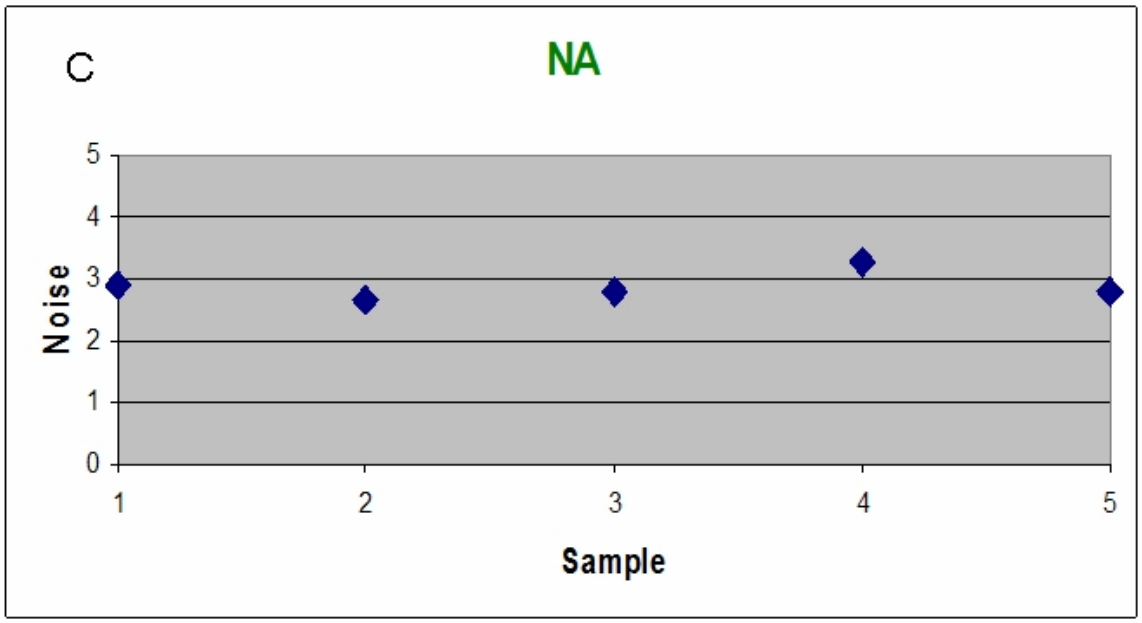
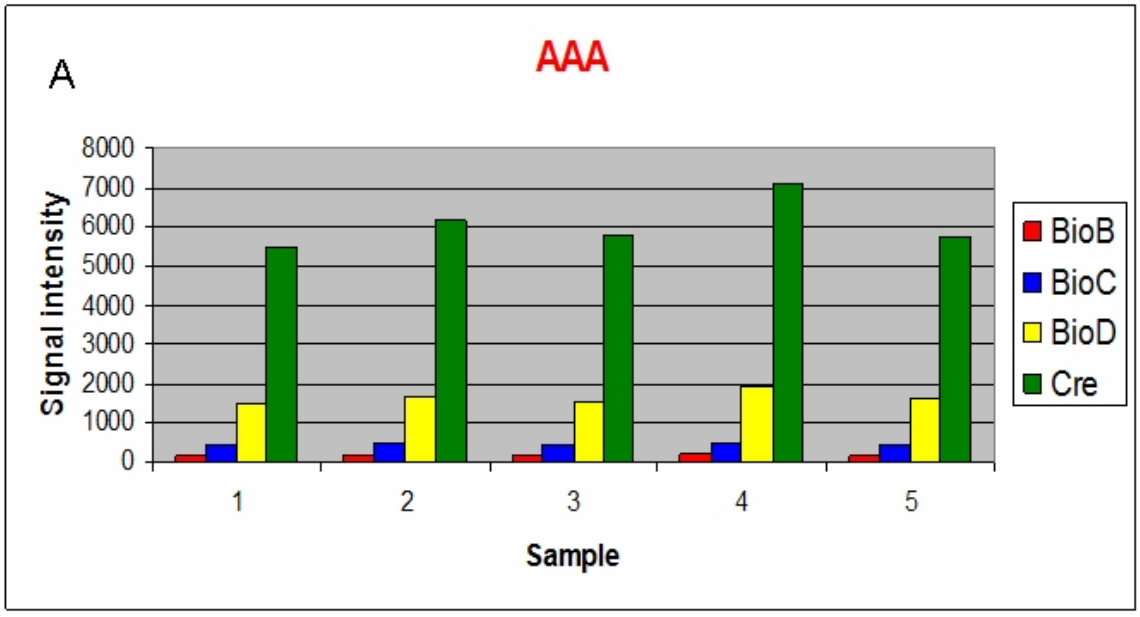
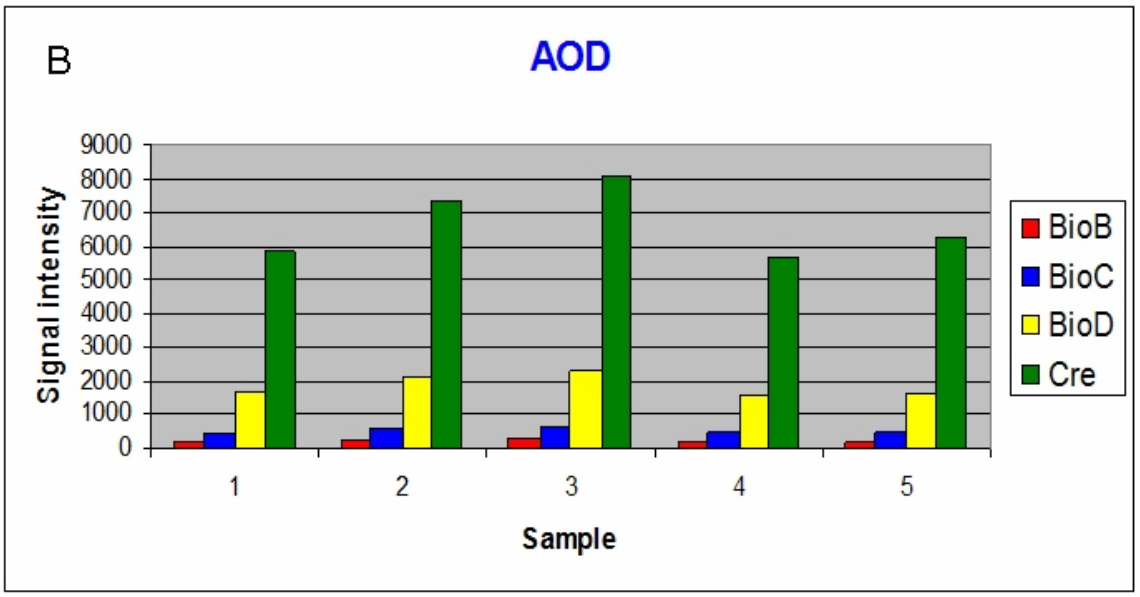


Figure 3.13 Noise values for A) AAA, B) AOD and C) Normal artery.

3.4.5 Hybridisation controls: bioB, bioC, bioD and Cre

BioB was present in all 15 samples indicating a high sensitivity for all the assays. Each sample showed increased signal intensities for bioB, bioC, bioD and Cre respectively reflecting their staggering concentrations. This step confirmed that hybridisation was successful in every sample (Figures 3.14 A, B and C).





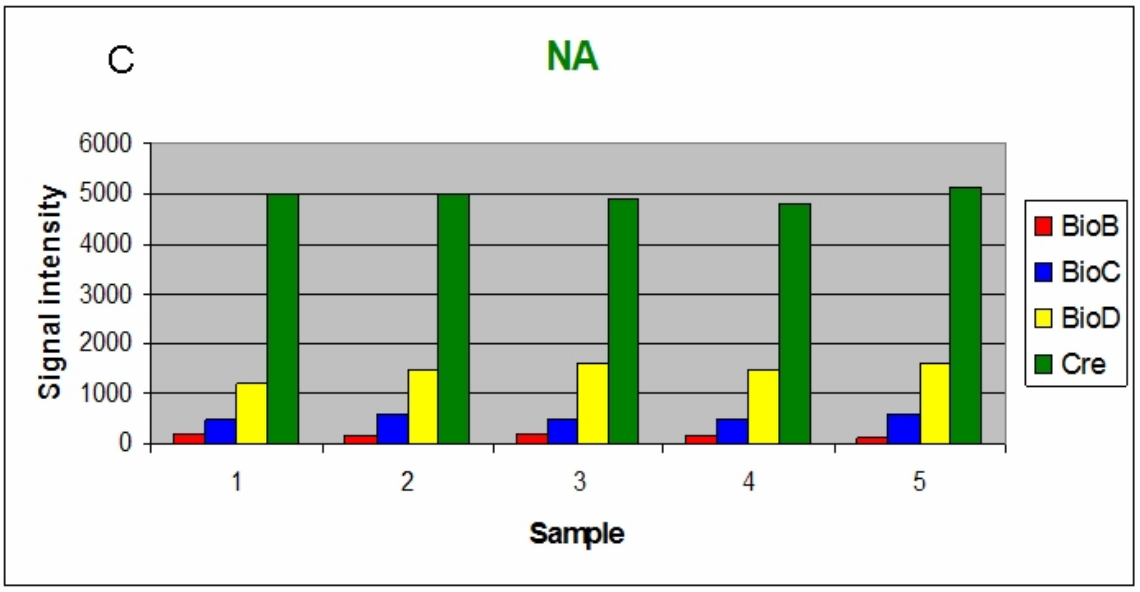
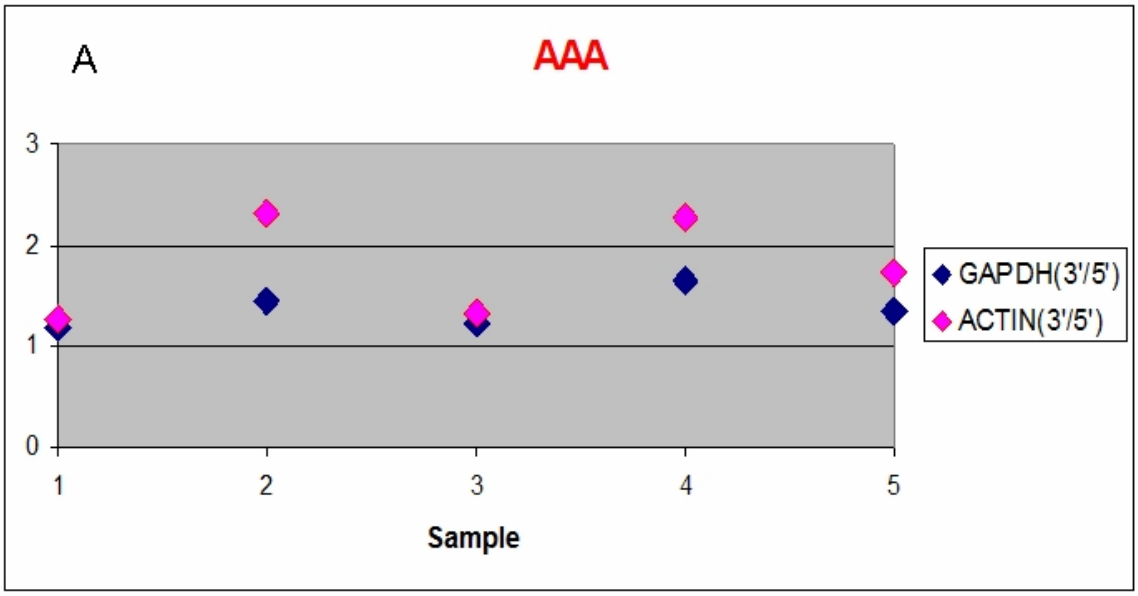
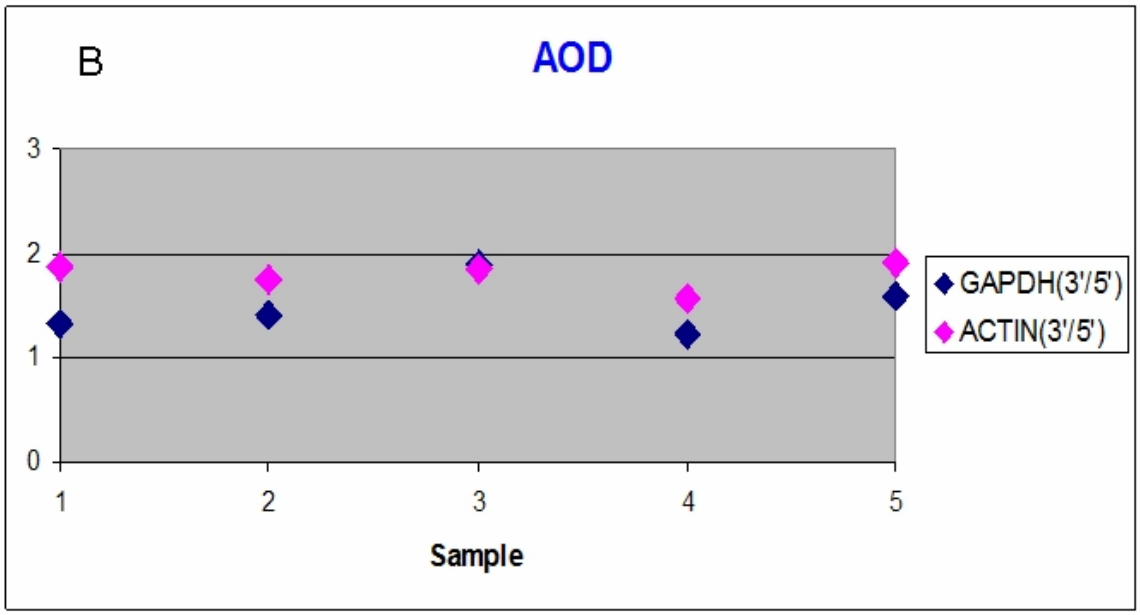


Figure 3.14 Hybridisation controls for A) AAA, B) AOD and C) Normal artery.

3.4.6 Internal control genes

3'/5' ratios for both GAPDH and β-Actin were less than 3.0 in all the samples used. This indicates that good quality RNA was used for all the samples which would result in reduced non-specific hybridisation.





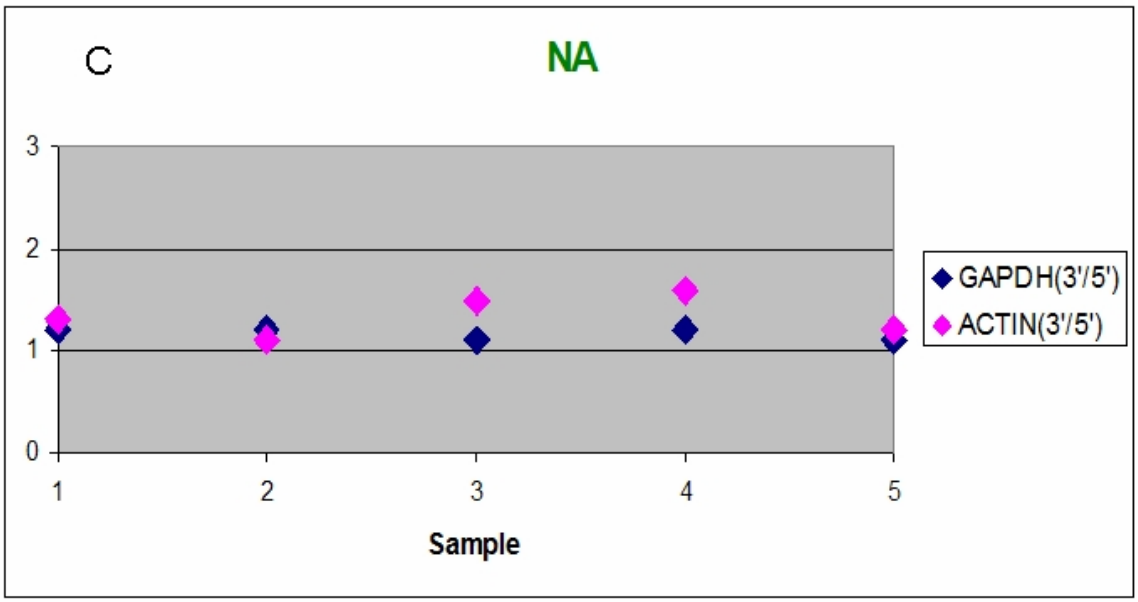
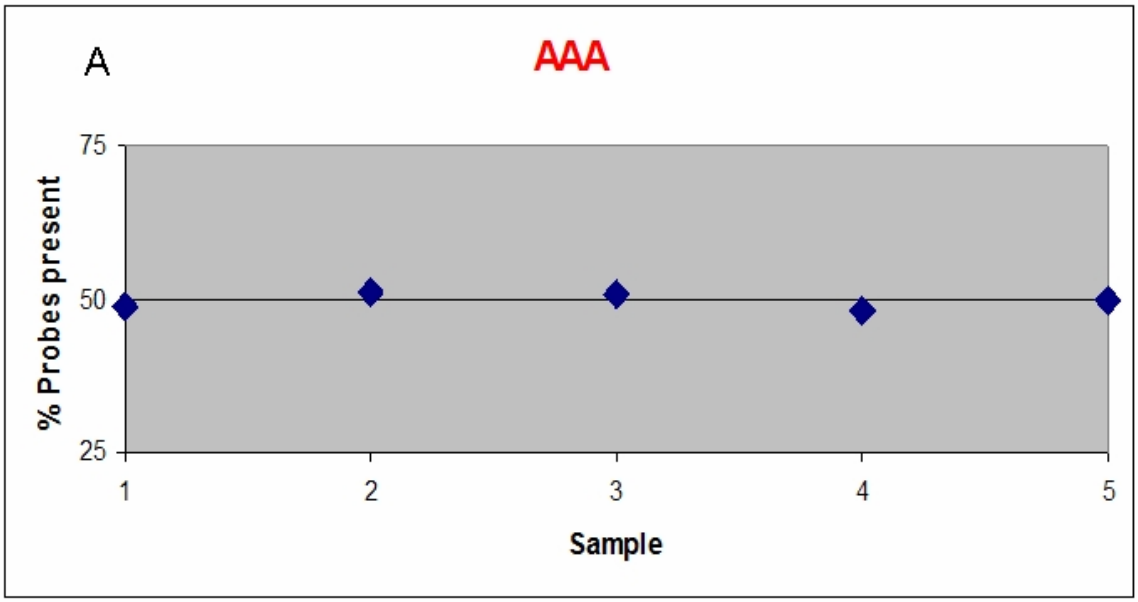
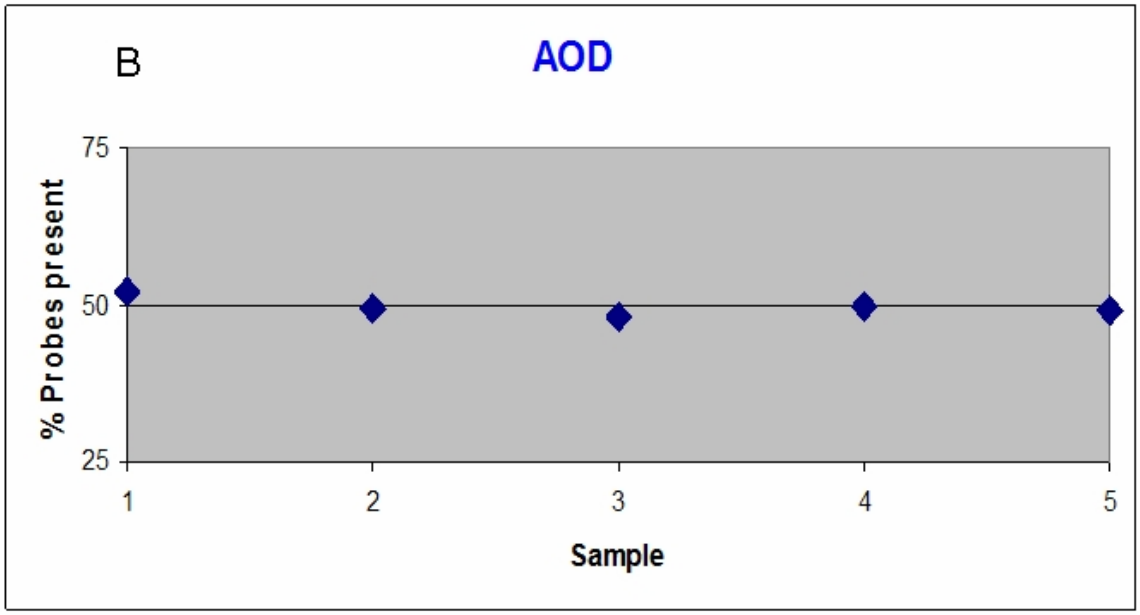


Figure 3.15 3'/5' ratios of housekeeping genes for A) AAA, B) AOD and C) Normal artery.

3.4.7 Percent probe present

The percentage of probes called 'Present' was about 50% in each sample with minimal variation between samples.





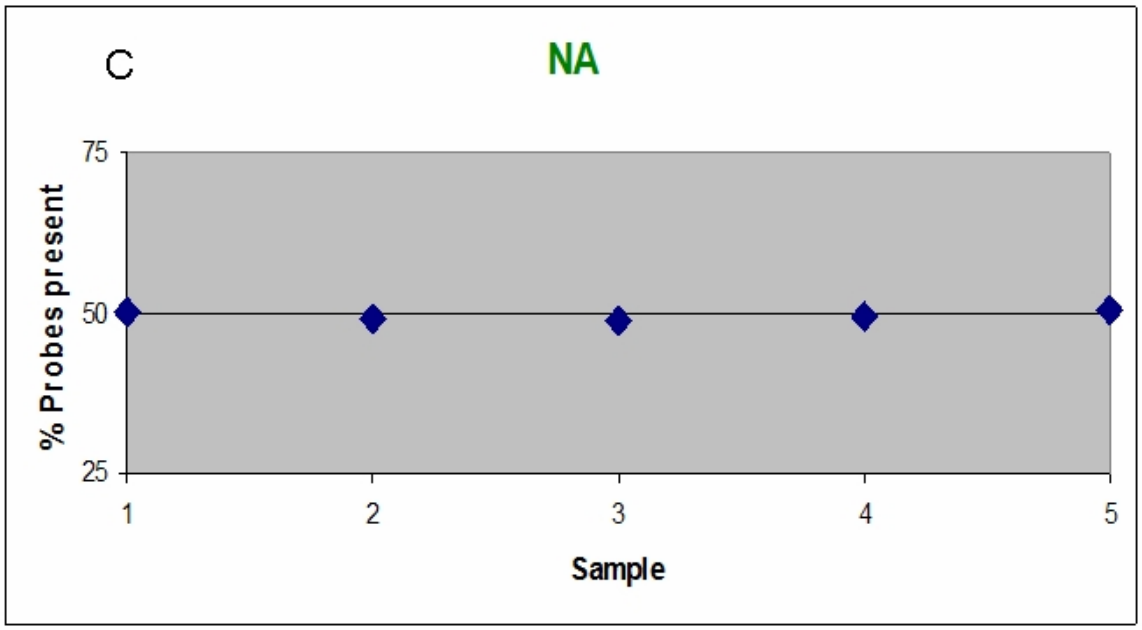
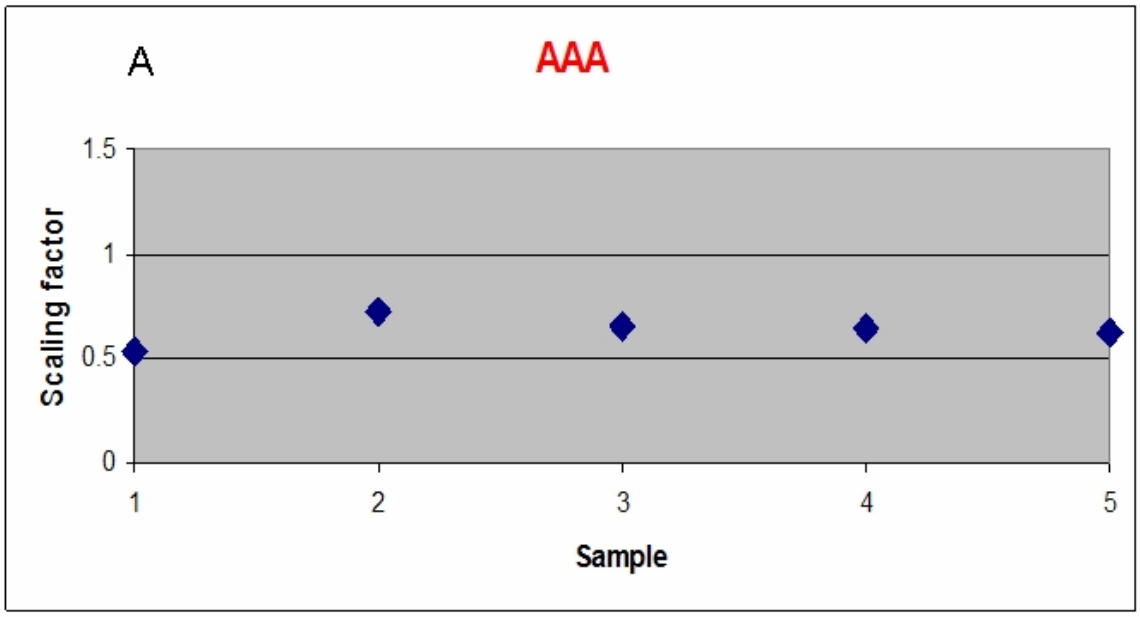
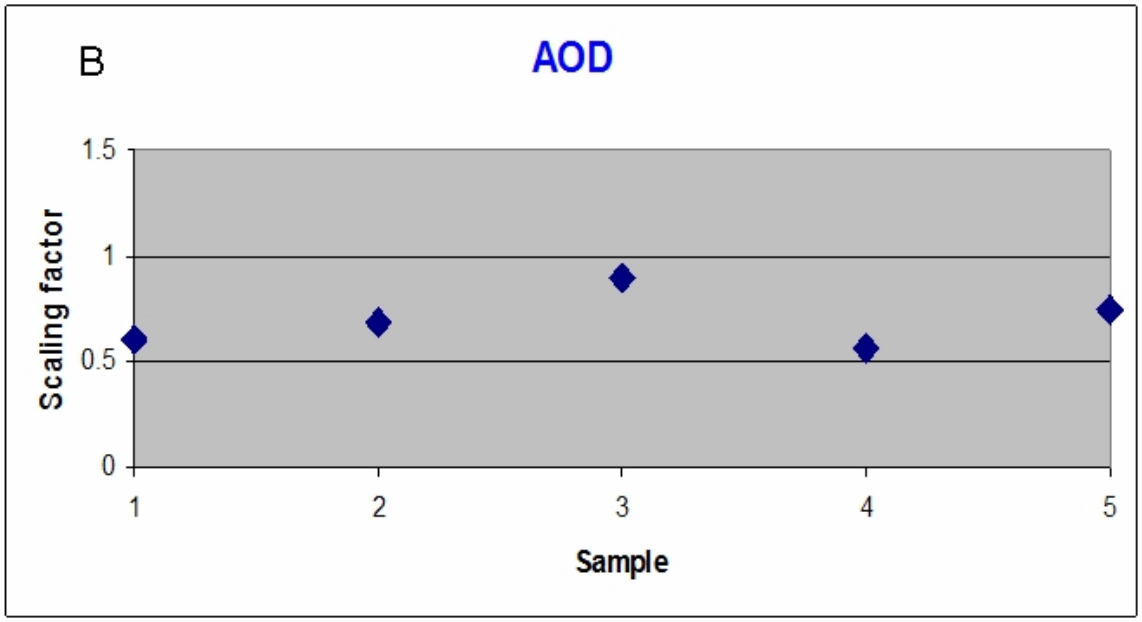


Figure 3.16 Percentage of probes present for A) AAA, B) AOD and C) Normal artery.

3.4.8 Scaling factor

The scaling factors for all the 15 samples were within 3-fold of each other making them suitable for statistical comparison (Figures 3.17 A, B and C).





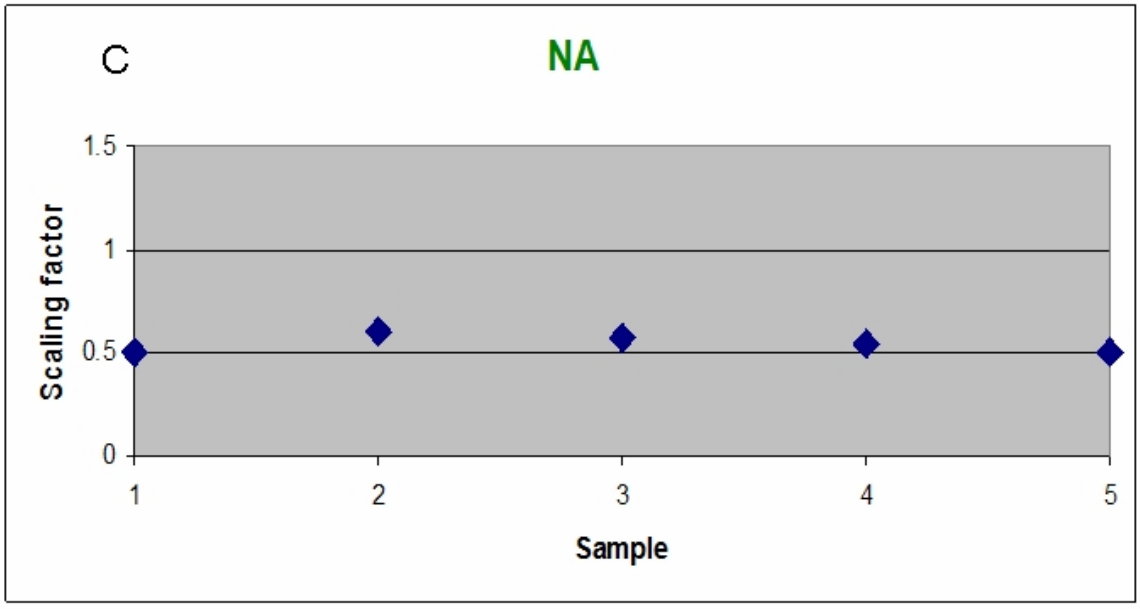


Figure 3.17 Scaling factors for A) AAA, B) AOD and C) Normal artery.

3.5 Discussion

The quality control step is crucial in ensuring that all the samples satisfy the stringent criteria as set out by the chip manufacturer (Affymetrix). All the quality control parameters investigated were within normal limits for all 15 samples employed in this study. The variations in the RIN numbers of the RNA used for the samples did not appear to affect the micro-array experiment as evidenced by the 3'/5' ratios of GAPDH and β-Actin which were <3 for all samples, indicating minimal degradation. The quality of the scanned images was therefore acceptable for further statistical analysis[276].

Chapter 4

Biostatistical analysis: differential expression.

4.1 Introduction

Microarray experiment generates a large volume of data. Different software packages (GeneSpring, Genemaths XT, Genesifter, and Spotfire) are available for data analysis to determine significant target genes. The principle of the analysis is, however, the same and involves the following steps:

i) Normalisation: A normalised value represents a relative intensity resulting from division of a raw value (signal intensity derived from microarray experiment) by a control value. The control value is the value by which the raw intensities are divided to normalise the data and centre them on 1. Types of normalisation applied in this study are detailed in section 4.2.1.

ii) Principal component analysis (PCA): This is a decomposition technique that reduces the multi-dimensionality of a data set to allow visual analysis. Dimension is defined as the minimum number of coordinates needed to specify each point. Since visual analysis is performed in three dimensions, in a coordinate system of x, y and z, PCA allows reduction of a matrix of any dimensionality to only three dimensions[281].

iii) Clustering: This is the assignment of a set of observations into subsets (called clusters) so that observations in the same cluster are similar in some sense[282]. Clustering technique used in this study is detailed in Section 4.2.2.

iv) Statistical analysis: This is detailed in Section 4.2.4.

v) Classification according to GO (Gene ontology) processes: The GeneSpring software (version 7.3.1, Agilent technologies) was used to analyse the microarray data in this study.

4.2 Methods

The microarray data from all the samples were imported into the GeneSpring software (Agilent technologies). Two comparisons were carried out: AAA vs. AOD and AAA vs. NA. The data was analysed systematically using the following steps as detailed out by GeneSpring.

4.2.1 Normalisation

The data was first normalised to ensure consistency in terms of biological and non-biological variations between the samples. Normalisation was carried out in the following order:

i) Data transformation. Measurements less than 0.01 were set to 0.01 as GeneSpring uses log values for comparison.

ii) Per chip normalisation to 50%. This step controlled for variation in intensity across the chips, caused by non-biological variations such as inconsistencies in washing and staining of the chips on the fluidics station.

iii) Per gene normalisation to median. This accounted for differences in detection efficiency between spots. The relative change in expression level was compared using the formula:

(Signal strength of gene A in sample / Median of expression of gene A in all the samples)

4.2.2 Quality control

This step is used to determine whether variations within the data are due to methodological differences rather than biological variations. This step is crucial prior to statistical analysis.

i) Normalisations. After the normalisation steps described above, all the samples and their distributions around 1 were analysed. Replicates for the same condition should have similarly shaped normalisation curves around 1.

ii) Principal Component Analysis (PCA). The data from expression arrays are of high dimensionality. In this experiment, 54000 transcripts were measured in 15 patients, generating a matrix of 15 × 54000. It is impossible to analyse for trends in such a matrix by visual inspection. PCA is a decomposition technique that reduces the dimensionality of the data into a new set of variables (principal components) to summarise the essential features of the data. The first component accounts for maximum variability between conditions. It gives a general view of the variation between replicates[281;283].

iii) Hierarchal clustering. This clustering technique shows how similar the samples are based on their gene expression profiles. This is based on

correlations between the samples. For true reflection of the correlation, the 'per gene normalisation step' (Section 4.2.1) is removed prior to cluster analysis otherwise samples will look artificially close. Pearson's correlation which assumes a normal distribution and equality of variances is most commonly used. The variance assumption has, however, been shown to be a cofounder in microarray analysis and thus a more conservative correlation measure that makes use of ranked data namely the Spearman's correlation was used[282;284]. A distance measure corresponding to the Spearman ranked correlation is computed as follows[285]:

$$d_s = 1 - r_s$$

d_s - distance based on Spearman correlation

r_s - Spearman rank correlation.

Samples that represent the same disease should cluster together. This technique may fail if there are a large number of genes in the order of several thousands[282].

4.2.3 Generating list of genes of interest

Once the samples had passed the quality control steps above, they were analysed for biological variation. Genes that were consistently differentially expressed by at least two-fold when comparing either AAA vs. AOD or AAA vs. NA were identified using the filters described below.

i) Genes that were called 'Present' or 'Marginal' in 4 out of 10 samples. This filter allowed all genes that were 'Present' or 'Marginal' in 4 out of 10 samples in the microarray data to be included for further analysis thus ensuring that only genes that are consistently differentially expressed were included for further analysis.

ii) Standard deviation (SD) filter. Only genes that varied by less than 1.5 SD around their mean of expressions of the replicates were considered. Genes with a high variance are likely to be less reliable.

iii) Fold change of 2. Only genes that were differentially expressed by at least 2-fold were included[95;135;145;258].

The purpose of applying these filters was to generate a set of reliable genes for further analysis and to decrease the number of false positives that passed through the filters following statistical analysis.

4.2.4 Statistical analysis

A one-way ANOVA with a parametric t-test was used to identify genes that were differentially expressed ($P < 0.05$) after Benjamini-Hochberg correction test (false discovery rate = 0.05) to decrease the false discovery rate in a large gene set. A parametric t-test was used as all the data were normalised and showed normal distribution curves prior to statistical analysis (sections 4.2.1 and 4.3.1).

4.2.5. Gene ontology

Differentially expressed genes were analysed in terms of their molecular functions. Genes were grouped into the following categories: proteolysis, immune response, apoptosis and angiogenesis.

4.2.6 Identifying genes on chromosomes 19q13 and 4q31

Genes on chromosomes 19q13 and 4q31 were identified. These chromosomes have been identified as susceptible loci for AAA genes in linkage studies[240].

4.3 Results

4.3.1 Normalisations

Both normalisation curves comparing AAA vs. AOD, or AAA vs. NA showed similar shapes for replicates. All the samples normalised around 1 as would be expected (Figures 4.1 A and B respectively).

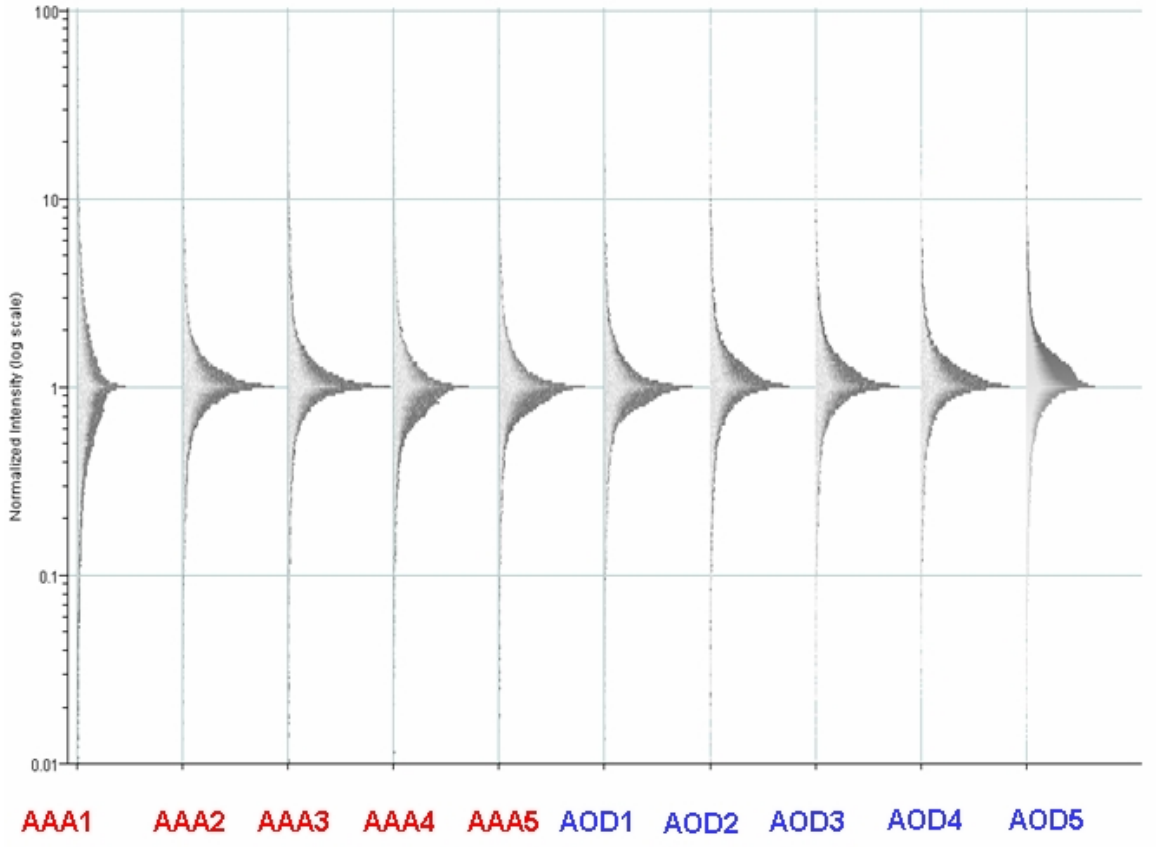


Figure 4.1A Normalisation of AAA vs. AOD samples.

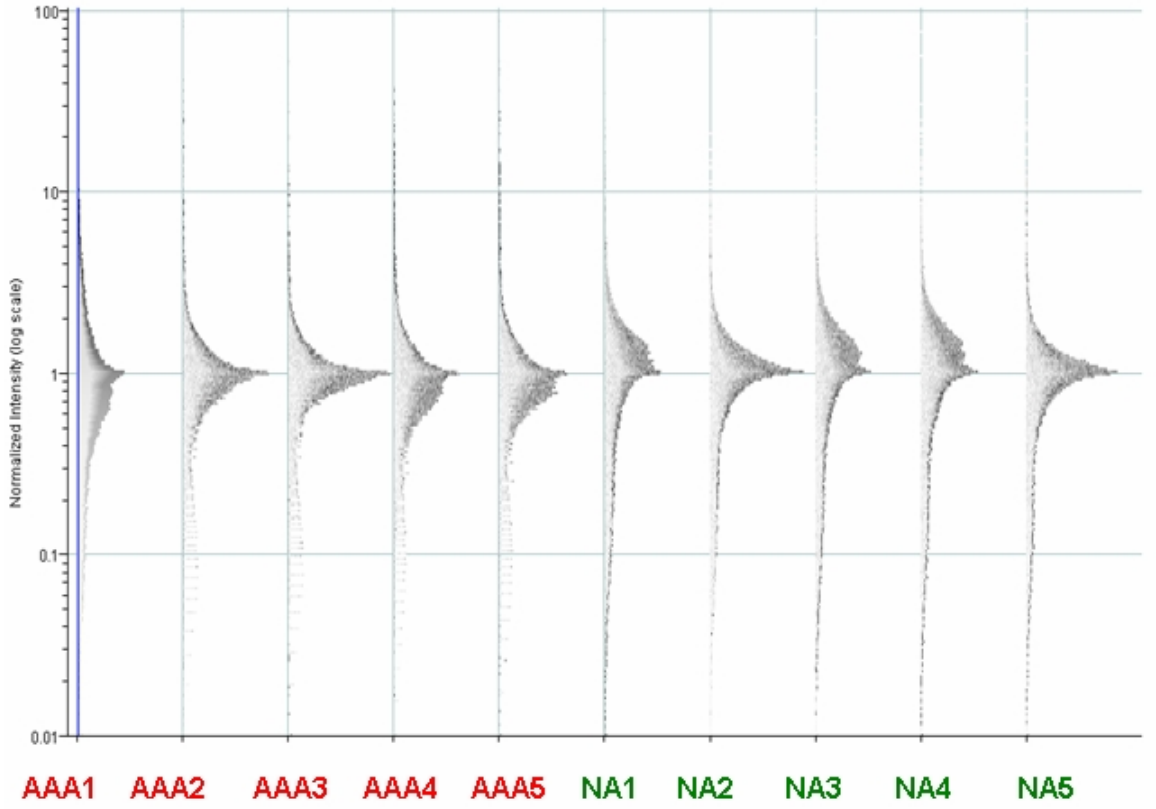
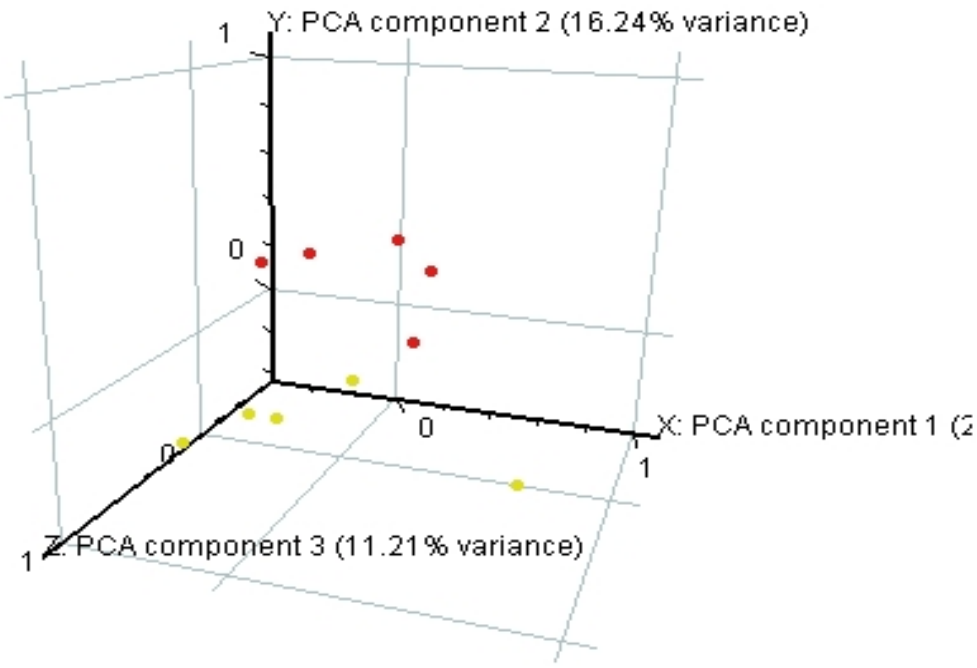


Figure 4.1B Normalisation of AAA vs. NA samples.

4.3.2 Principal component analysis

This helps to visually identify samples that are outliers for a given condition. Comparison of AAA vs. AOD (Figure 4.2A) showed that all the AOD replicates clustered together. Similarly with the exception of one sample the AAA replicates clustered together. The matrix for the outlying sample lies in the XZ plane as the other AAA replicates compared to the AOD replicates which lie in the XY plane indicating closer similarity to the AAA samples. Comparison of AAA and NA

samples (Figure 4.2B), there revealed 2 distinct group of matrices representing each condition.



X-axis:	PCA component 1 (28.47% v...	Conditions:	AAAvsAOD, All Samples
Y-axis:	PCA component 2 (16.24% v...	Colored by:	Parameter Tissue Type
Z-axis:	PCA component 3 (11.21% v...		

Figure 4.2A Principal components showing variances between AAA replicates (yellow) and AOD replicates (red).

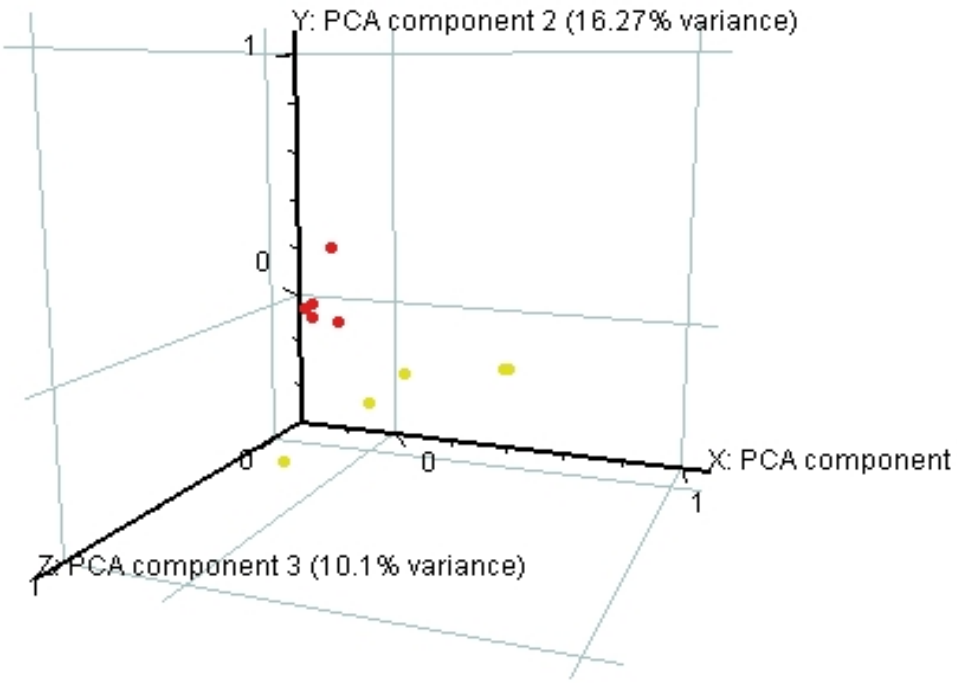


Figure 4.2B Principal components showing variances between AAA replicates (red) and NA replicates (yellow).

4.3.3 Hierarchal clustering

Similarity of gene expression between replicates of AAA and AOD can be visualised by hierarchal clustering using Spearman correlation. The data is represented using a dendogram with a colour coded matrix for gene expression. The colour intensity reflects gene expression level of a particular gene within a sample. The samples are then clustered according to their similarities based on Euclidian distance. One of the AAA replicates in Figure 4.3A clusters as a separate branch. This can account for biological variation (family history of AAA as opposed to spontaneous AAA) and this sample was included in the analysis as it shows a closer similarity to AAA replicates rather than AOD replicates (d_s = 0.792 compared with other AAA samples and d_s = 0.501 compared with other AOD samples, p=0.04). Figure 4.3B shows that AAA and NA replicates cluster according to the conditions they represent.

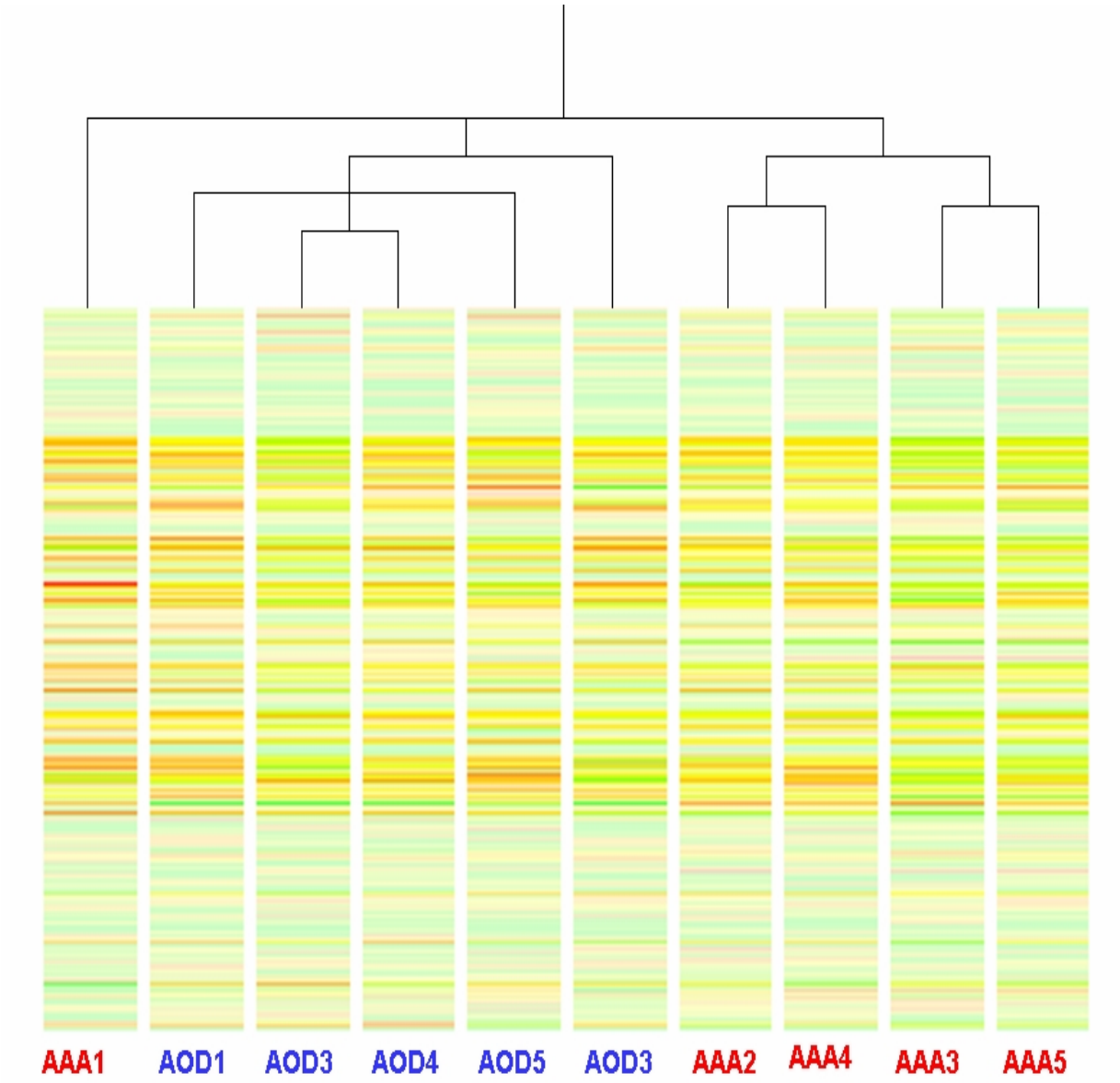


Figure 4.3A Hierarchal clustering of AAA and AOD replicates.

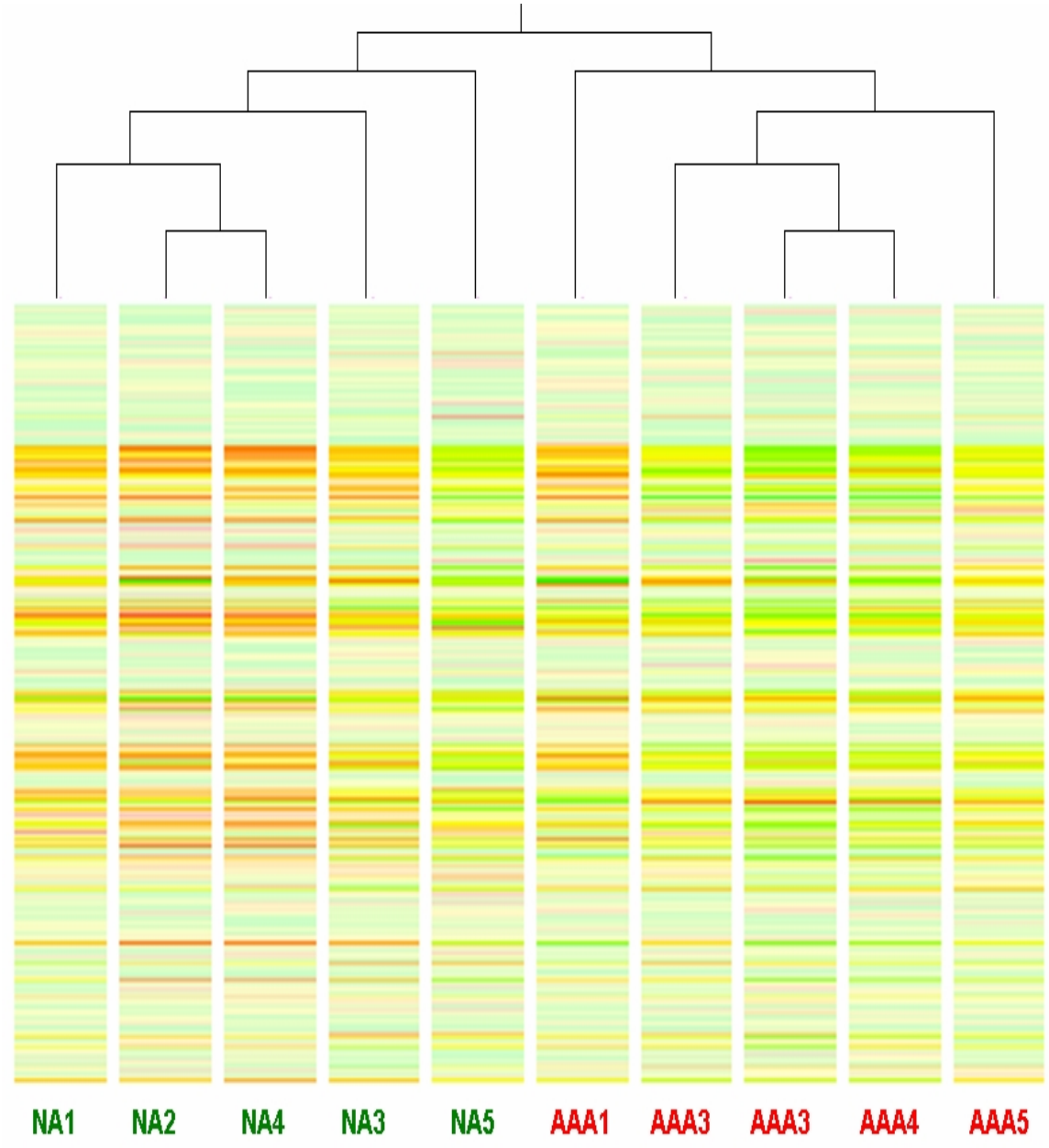


Figure 4.3B Hierarchal clustering of AAA and NA replicates.

4.3.4 Filtering for genes of interest

The genes of interest were generated using the steps described in section 4.2.3. Each step eliminated genes that were potentially unreliable. As shown in Table 4.1 below, the number of transcripts that were entered in the statistical analysis was significantly lower than the 54,675 originally present.

Table 4.1 Genes of interest identified when comparing gene expression of AAA with AOD and NA.

	Number of transcripts	
Filters applied	**AAA vs. AOD**	**AAA vs. NA**
Total	54 675	54 675
Present or Marginal 4/10	29 141	31426
Standard deviation_ 1.5	28 630	31075
Fold change > 2	1 126	6855

4.3.5 Statistical analysis

Statistical analysis was carried out as described in section 4.2.4. The numbers of differentially expressed genes when comparing AAA with AOD or NA are shown in Table 4.2. The top 30 genes with the greatest fold change are shown in Tables 4.3 and 4.4 (AAA vs. AOD) and Tables 4.5 and 4.6 (AAA vs. NA) respectively and details of the remaining genes are given in Appendixes B-E.

Table 4.2 Number of differentially expressed genes when comparing AAA with AOD and NA.

Differential expression	AAA vs. AOD	AAA vs. NA
Total	337	3900
Upregulated	144	777
Downregulated	193	3123

Table 4.3 Upregulated genes for AAA vs. AOD.

	Gene Description	Gene symbol	Fold change
1	Polycystic kidney and hepatic disease 1 (autosomal recessive)-like 1	PKHD1L1	32
2	Ig kappa chain precursor V region - human (fragment)	LOC391427	23
3	Stathmin-like 2	STMN2	22
4	Immunoglobulin heavy locus		18
5	Similar to Ig kappa chain	LOC339562	15
6	Similar to omega protein	LOC91353	14
7	Immunoglobulin lambda joining 3	IGLC2	14
8	Claudin 11	CLDN11	12
9	Hook homolog 1 (Drosophila)	HOOK1	12
10	Immunoglobulin kappa variable 1D-13	IGKV1D-13	11
11	BCR downstream signaling 1	BRDG1	10
12	UDP-Gal:beta 1,3-galactosyltransferase, polypeptide 2	B3GALT2	9
13	Immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	IGJ	8
14	Membrane-spanning 4-domains, subfamily A, member 1	MS4A1	7

15	Bagpipe homeobox homolog 1 (Drosophila)	BAPX1	6
16	CD79A antigen (immunoglobulin-associated alpha)	CD79A	6
17	Pre-B lymphocyte gene 3	VPREB3	6
18	Fc receptor-like 1	FCRL1	6
19	Fc receptor-like 2	FCRL2	6
20	Paired box gene 5 (B-cell lineage specific activator)	PAX5	5
21	Membrane-spanning 4-domains, subfamily A, member 1	MS4A1	5
22	Major histocompatibility complex, class II, DO beta	HLA-DOB	5
23	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	5
24	Homeo box D10	HOXD10	4
25	Signal peptide, CUB domain, EGF-like 2	SCUBE2	4
26	Spi-B transcription factor (Spi-1/PU.1 related)	SPIB	4
27	Papilin, proteoglycan-like sulfated glycoprotein	PAPLN	4
28	C1q and tumor necrosis factor related protein 7	C1QTNF7	4
29	Complement component 3	C3	4
30	CD19 antigen	CD19	4

Table 4.4 Downregulated genes for AAA vs.AOD.

	Gene Description	Gene Symbol	Fold Change
1	peroxidasin homolog-like (Drosophila)	PXDNL	10
2	SPOC domain containing 1	SPOCD1	10
3	aortic preferentially expressed gene 1	APEG1	8
4	angiopoietin-like 4	ANGPTL4	7
5	heme oxygenase (decycling) 1	HMOX1	7
6	solute carrier family 16 (monocarboxylic acid transporters), member 10	SLC16A10	5
7	collagen, type V, alpha 3	COL5A3	5
8	PDZ and LIM domain 3	PDLIM3	4
9	Effector cell peptidase receptor 1	BIRC5	4
10	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	ITGA5	4
11	Spermidine/spermine N1-acetyltransferase	SAT	4
12	folate hydrolase (prostate-specific membrane antigen) 1	FOLH1	4
13	collagen, type XVIII, alpha 1	COL18A1	4
14	PDZ binding kinase	PBK	3

15	Endothelin receptor type A	EDNRA	3
16	endothelial differentiation, sphingolipid G-protein-coupled receptor, 3	EDG3	3
17	Sulfatase 1	SULF1	3
18	fibronectin 1	FN1	3
19	collagen, type V, alpha 3	COL5A3	3
20	Ribosomal protein S7	NSF	3
21	LIM and senescent cell antigen-like domains 3	LIMS3	3
22	adipose differentiation-related protein	ADFP	3
23	Protocadherin 17	PCDH17	3
24	solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	SLC7A11	3
25	SH3-domain GRB2-like (endophilin) interacting protein 1	DKFZp761D221	3
26	tumor necrosis factor, alpha-induced protein 6	TNFAIP6	3
27	ATP-binding cassette, sub-family C (CFTR/MRP), member 3	ABCC3	3
28	collagen, type I, alpha 1	COL1A1	3
29	angiotensinogen (serpin peptidase inhibitor, clade A, member 8)	AGT	3
30	lysyl oxidase-like 2	LOXL2	3

Table 4.5 Upregulated genes for AAA vs. NA.

	Gene Description	Gene symbol	Fold change
1	Dystrobrevin, beta	DTNB	88
2	Immunoglobulin lambda joining 3	IGLC2	79
3	Similar to Ig kappa chain precursor V region	LOC391427	62
4	Fc receptor-like and mucin-like 1	FCRLM1	58
5	Immunoglobulin kappa variable 1-5	IGKC	55
6	Immunoglobulin lambda variable 3-25	IGLV3-25	52
7	Similar to omega protein	LOC91353	50
8	Immunoglobulin heavy constant mu	IGHM	50
9	Immunoglobulin kappa constant	IGKC	47
10	Coiled-coil domain containing 4	CCDC4	47
11	Immunoglobulin lambda variable 2-14	IGLV2-14	42
12	Fc receptor-like 1	FCRL1	39
13	Immunoglobulin heavy constant gamma 1 (G1m marker)	IGHG1	38
14	CD79A antigen (immunoglobulin-associated alpha)	CD79A	36

15	Similar to Ig kappa chain	LOC339562	34
16	Immunoglobulin kappa variable 1D-13	IGKV1D-13	29
17	Protein kinase (cAMP-dependent, catalytic) inhibitor alpha	PKIA	21
18	Polycystic kidney and hepatic disease 1 (autosomal recessive)-like 1	PKHD1L1	21
19	Immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	IGJ	20
20	SLAM family member 7	SLAMF7	19
21	BCR downstream signaling 1	BRDG1	17
22	Wingless-type MMTV integration site family, member 16	WNT16	15
23	Suppression of tumorigenicity 18 (breast carcinoma) (zinc finger protein)	ST18	15
24	T-cell activation GTPase activating protein	TAGAP	15
25	CD19 antigen	CD19	15
26	Class-I MHC-restricted T cell associated molecule	CRTAM	14
27	Fas apoptotic inhibitory molecule 3 ; Fas apoptotic inhibitory molecule 3	FAIM3	13
28	Regulator of G-protein signalling 13	RGS13	13
29	CD69 antigen (p60, early T-cell activation antigen)	CD69	12
30	Carbopeptidase Z	CPZ	12

Table 4.6 Downregulated genes for AAA vs. NA.

	Gene Description	Gene Symbol	Fold change
1	aortic preferentially expressed gene 1	APEG1	56
2	chromosome 6 open reading frame 168	C6orf168	24
3	neuronal pentraxin II	NPTX2	16
4	ATPase, Na+/K+ transporting, alpha 2 (+) polypeptide	ATP1A2	16
5	G protein-coupled receptor 37 (endothelin receptor type B-like)	GPR37	16
6	ADAM metallopeptidase with thrombospondin type 1 motif, 8	ADAMTS8	15
7	transient receptor potential cation channel, subfamily C, member 4	TRPC4	14
8	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 4	PPFIA4	14
9	chromosome 14 open reading frame 132	C14orf132	14
10	receptor-interacting serine-threonine kinase 4	RIPK4	13
11	microsomal triglyceride transfer protein (large polypeptide, 88kDa)	MTP	13
12	thyroid hormone receptor, alpha (erythroblastic leukemia viral (v-erb-a) oncogene homolog, avian)	THRA	12
13	chromosome 8 open reading frame 46	C8orf46	12
14	E2a-Pbx1-associated protein	EB-1	12

15	Astrotactin 2	ASTN2	12
16	neurotrophic tyrosine kinase, receptor, type 3	NTRK3	12
17	metallophosphoesterase domain containing 2	MPPED2	12
18	ryanodine receptor 2 (cardiac)	RYR2	12
19	attractin-like 1	ATRNL1	11
20	integrin, alpha 10	ITGA10	11
21	neurotrophic tyrosine kinase, receptor, type 3	NTRK3	11
22	copine IV	CPNE4	11
23	calsequestrin 2 (cardiac muscle)	CASQ2	10
24	purinergic receptor P2Y, G-protein coupled, 2	P2RY2	10
25	betacellulin	BTC	10
26	leucine-rich repeat-containing G protein-coupled receptor 6	LGR6	10
27	transient receptor potential cation channel, subfamily C, member 4	TRPC4	9
28	caspase 12 pseudogene 1	CASP12P1	9
29	regulator of G-protein signalling 5	RGS5	9
30	leiomodin 1 (smooth muscle)	LMOD1	9

4.3.6 Gene ontology

Genes were classified according to their molecular functions in groups that reflected processes known to be important in AAA development. These included: proteolysis, inflammation, apoptosis and angiogenesis. Table 4.7 summarises the number of genes that are differentially expressed in each group when comparing AAA vs. NA or AAA vs. AOD. The differentially expressed genes between AAA and AOD and AAA and NA are shown in Appendix F and J (Inflammatory genes), G and K (Proteolytic genes), H and L (Apoptotic genes) and I and M (Angiogenic genes) respectively.

Table 4.7 Number of differentially expressed genes in pathological processes known to be associated with aneurysmal disease.

Pathological process	AAA vs. NA		AAA vs. AOD	
	Up	Down	Up	Down
Inflammation	144	48	31	9
Proteolysis	110	253	10	20
Apoptosis	23	50	6	6
Angiogenesis	4	11	3	5

The expressions of the following proteolytic genes, which have been previously investigated at our laboratory: MMP-3, MMP-9 and Cathepsin H are shown in figures 4.4–4.6 respectively. Both MMP-3 and Cathepsin H were up-regulated in AAA compared with AOD and NA. MMP-9 showed no significant change between AAA and AOD but significantly higher expression in AAA compared with NA in this microarray experiment.

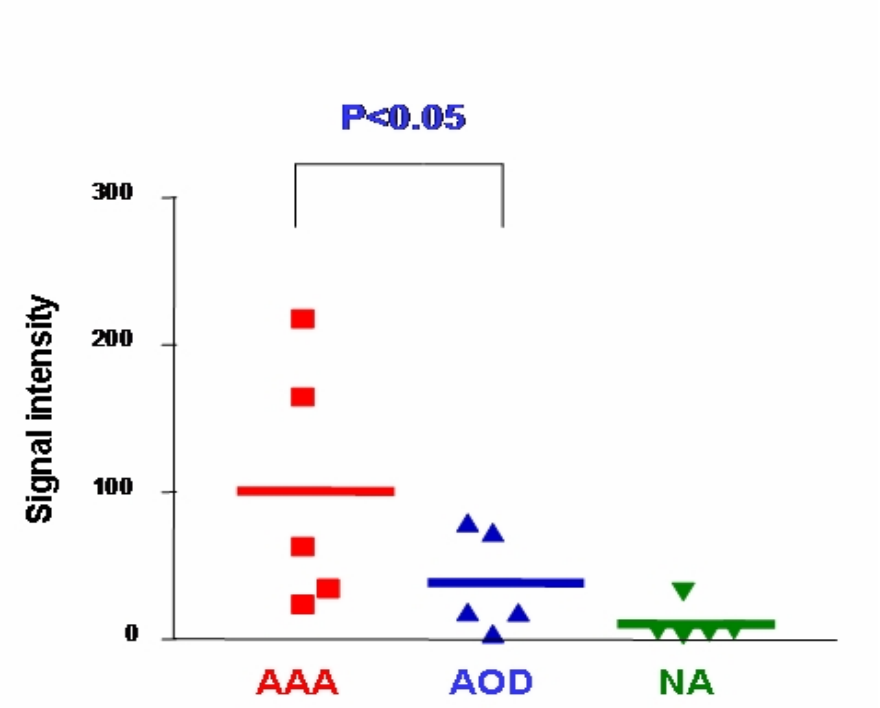


Figure 4.4 Microarray analysis derived MMP-3 expression.

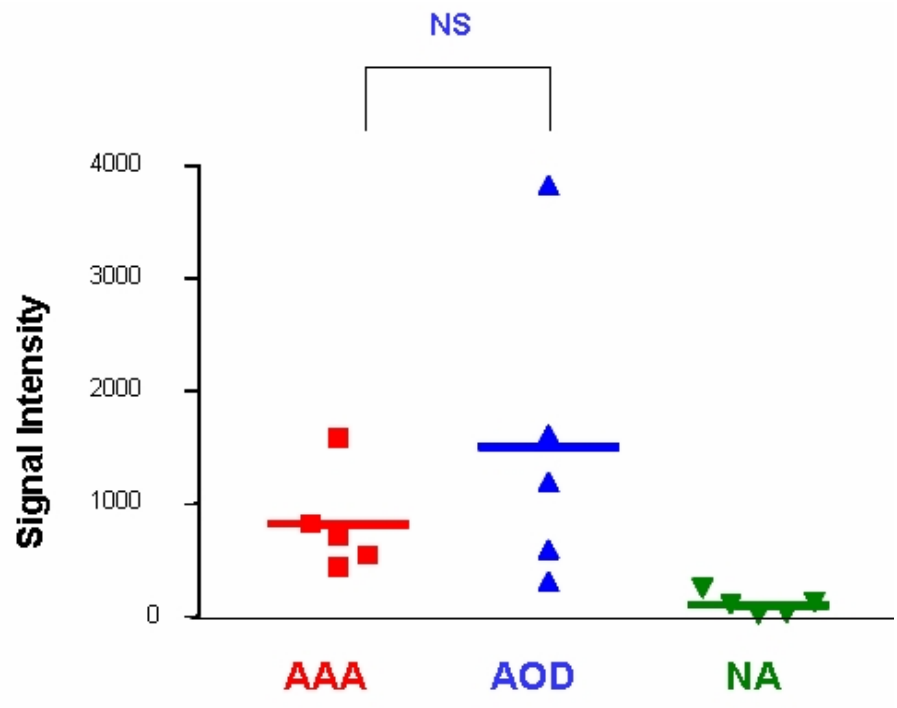


Figure 4.5 Microarray analysis derived MMP-9 expression.

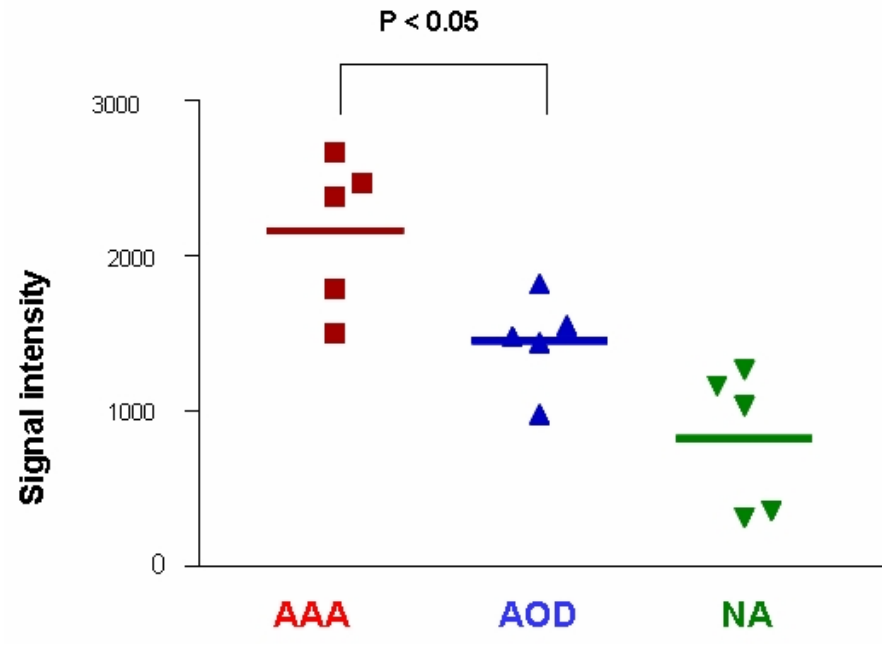


Figure 4.6 Microarray analysis derived Cathepsin H expression.

4.3.7 Genes differentiated on chromosome 19q13

CD79A, Spi-B transcription factor (Figures 4.7–4.8) and ryanodine receptor 1 (RYR1) were upregulated in AAA compared with AOD. No gene was differentially expressed on chromosome 4q31.

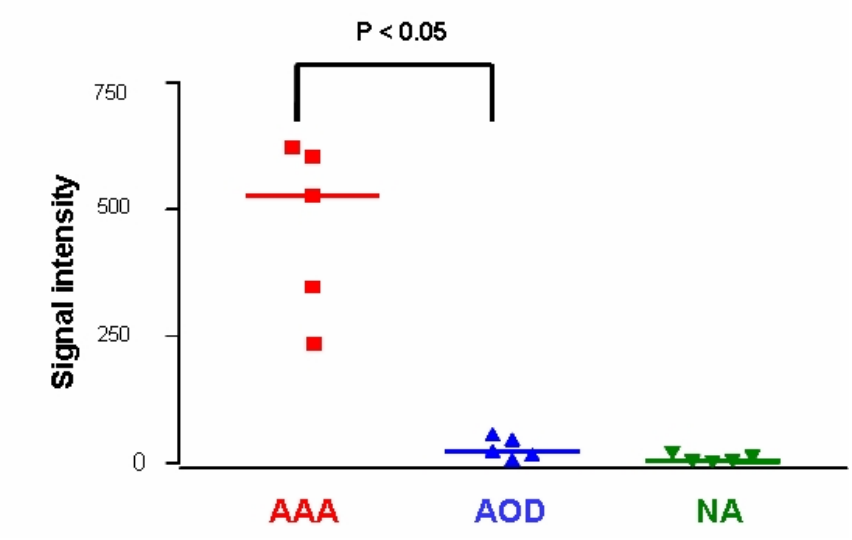


Figure 4.7 Microarray analysis derived CD79A expression.

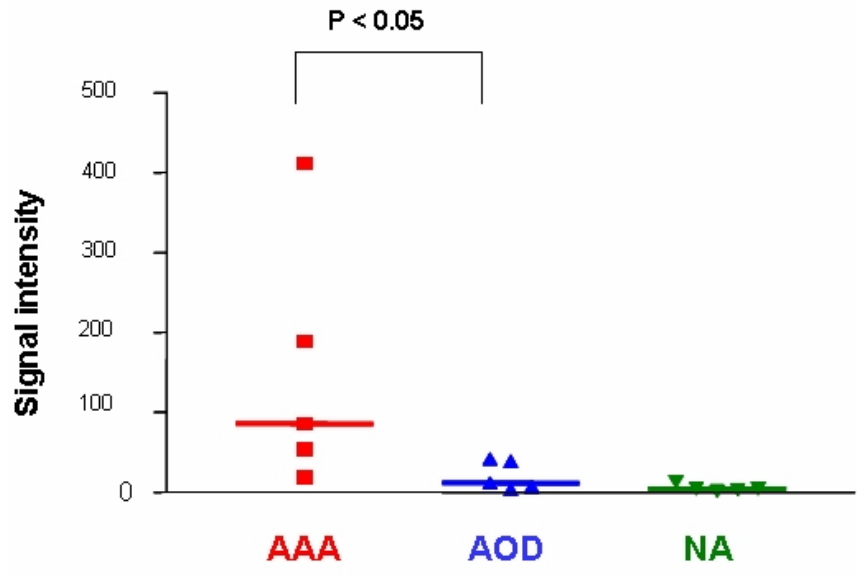


Figure 4.8 Microarray analysis derived Spi-B transcription factor expression.

4.4 Discussion

The quality control steps carried out in this Affymetrix whole genome gene chip analysis of gene expression in AAA, AOD and NA walls have satisfied the requirements for statistical analysis. When comparing AAA with NA, there were a ten-fold greater number of genes that were differentially expressed than in the AAA vs. AOD group. Atherosclerosis is a consistent finding in the walls of AAA[153]. Comparison of gene expression in AAA wall with that in the wall of AOD is intuitively more relevant as this removes genes associated with atherosclerosis from the analysis[123] and may highlight genes that are important in AAA development only.

The data from this whole genome analysis confirms that of previous studies in which AAA was compared with AOD. Carrell et al[123] showed that MMP-3 was differentially expressed when comparing AAA with AOD and there was no difference for MMP-9 expression. Abisi et al[95] showed higher expression and activity of Cathepsin H only in AAA compared with AOD at the translational level. These results were reflected in our data (Figures 4.4–4.6).

The importance of inflammation in AAA is highlighted by the large number of inflammatory genes that were upregulated in both comparisons i.e. AAA vs. NA and AAA vs. AOD in this study. Among the genes with the highest fold-change (i.e. first 20 genes in either comparison), there was a predominance of inflammatory genes (55% in AAA vs. AOD and 75% in AAA vs. NA). A whole transcriptome analysis comparing AAA with NA[96] has also highlighted a predominance of overexpressed inflammatory genes in the AAA group.

The proteolytic genes represent the second largest group of differentially expressed genes in AAA compared with AOD or NA. Extracellular matrix degradation and remodelling is a component of both AAA and AOD[147;286]. Except for upregulation of MMP-3 and downregulation of MMP-14 none of the other MMPs or protease inhibitors was differentially expressed in our study. Similar results were shown by Armstrong et al[250] where they found no differential expression of MMPs or TIMPs in AAA compared with AOD using a limited microarray platform. Although MMP-9 is increased in both AAA and AOD compared with normal, its location in the aortic wall in both pathological processes differs. In AAA, MMP-9 is localised to the adventitia as compared with AOD where it is restricted to the media[286]. Interestingly, the proteolytic genes are predominantly downregulated when comparing AAA with AOD or NA. This may reflect the fact that the aneurysmal tissues used in this study were from large aneurysms and genes expressed at that stage of the disease pertains more to extracellular matrix remodelling rather than degradation. Also, the upregulated proteases are possibly those that do the most damage to the vessel wall.

Differential expression of genes present on chromosome 19q13 (a susceptible locus for aneurysm development)[240] was also found. Genes encoding CD79A (Figure 4.8) and Spi-B transcription factor (Figure 4.9) showed the highest fold change when comparing AAA against AOD or NA. CD79A is a B-cell surface receptor which has been implicated in haematological malignancies[287]. Spi-B is a transcription factor which is involved in determining haemopoetic lineage[288]. There were no differentially expressed genes on the other susceptible locus for AAA, chromosome 4q31[240].

Chapter 5

Quantitative Real Time Polymerase Chain Reaction (qRT-PCR).

5.1 Introduction

5.1.1 Overview of qRT-PCR

qRT-PCR has become widely established as a benchmark in the detection and quantification of RNA targets[289]. The ability to amplify the target sequence allows for greater sensitivity of detection than other RNA quantification techniques such as Northern blotting. Its reproducibility together with its potential for high throughput has seen it emerge as a key technology in identifying biomarkers, investigating molecular pathways and putative therapeutic targets. qRT-PCR based diagnostic assays are now available for a range of clinical conditions[290-292].

The following steps are involved in qRT-PCR:

1. appropriate quantification strategy;
2. reverse transcription of RNA to cDNA using a reverse transcriptase;
3. suitable detection chemistry to report the presence of PCR products;
4. monitoring of amplification in real-time and appropriate software for quantitative analysis.

5.1.2 Quantification strategies

There are two quantification methods: absolute (standard curve) and relative quantification[293]. Each is suitable for different applications.

i) Absolute quantification is based on the generation of a standard curve using a dilution series of an external standard. A linear plot of the log of the initial template

quantity against the C_t (threshold cycle) values for the standards is generated. The initial quantity of the unknown samples can then be determined by comparing their C_t values to the standard curve plot[293]. A variety of sources can be used as standard templates including plasmid containing a clone gene of interest, genomic DNA, cDNA, synthetic oligos or total RNA[291]. This strategy is important when the exact level of a template in the samples needs to be determined (e.g. the monitoring of viral load).

ii) Relative quantification refers to the relative concentration of the gene of interest in unknown samples compared to a calibrator or control sample. The calibrator is a baseline for the expression of a given target gene. The calibrator can be a time point, an untreated sample or a normal sample. Difference in the C_t (cycle threshold) values between an unknown sample and calibrator is expressed as fold changes (i.e. upregulated or downregulated) relative to the calibrator[294]. In order to control for variability in RNA isolation and in the efficiency of the reverse transcription step, the C_t value for each sample is normalised with a normalising reference gene(s) or target(s). A normalising gene is one whose expression is constant in both the experimental sample and the calibrator[294].

5.1.3 Choice of housekeeping genes for relative quantification

The identification of a valid housekeeping gene for data normalisation remains a very difficult and controversial problem. It is especially difficult when dealing with 'in vivo' samples and comparing gene expression patterns between different individuals[293]. The differences in cell composition between different samples could be responsible

for the observed fluctuations in overall gene abundance. Housekeeping genes that are considered to remain stable in a particular cell type under different conditions may be expressed at a different abundance level in a different cell type. Even if their expression remains stable in each cell type, differences in cell composition would reflect differences in the overall gene abundance.

Nine commonly used methods for normalising data, including a marker for 18s and eight housekeeping genes were assessed at our laboratory to identify the markers with the most stable expression levels across 35 different carotid plaque segments[258]. The stability of the housekeeping genes were measured using an *M* value as described by Vandesompele et al[295]. For every normalisation method, the pairwise variation with all other control genes was determined as the standard deviation of the logarithmically transformed expression ratios. The internal control gene-stability measure *M* was subsequently calculated as the average pairwise variation of a particular gene with all other control genes. Genes with the lowest *M* values had the most stable expression. The gene with the highest *M* value was excluded and *M* values were recalculated for all genes after each exclusion step. Assuming that the control genes are not co-regulated, stepwise exclusion of the gene with the highest *M* value resulted in a combination of three constitutively expressed housekeeping genes that have the most stable expression in the tested samples. GAPDH and β-actin were found to be the most stable housekeeping genes in this particular type of tissue (Table 5.1)[296].

Table 5.1 Order of stability of the nine normalisation methods according to their *M* values[296].

Housekeeping genes	*M* value
18s (ribosomal RNA)	2.19
HMBS (Hydroxymethyl-bilane synthase)	1.75
SHDA (Succinate dehydrogenase complex)	1.45
Cyclophilin	1.39
36B4 (human acidic ribosomal phosphoprotein)	1.20
TBP (TATA box binding protein)	0.80
B2M (Beta-2-microglobulin)	0.69
B-actin (Beta-actin)	0.57
GAPDH (Glyceraldehyde-3-phosphate)	0.57

5.1.4 Reverse transcription

One- step vs. two –step. qRT-PCR can be performed as either a one-step or two-step procedure. A one-step experiment is a single tube reaction that converts RNA to cDNA, followed by qPCR amplification using gene specific primers. A two-step experiment involves the initial conversion of RNA to cDNA followed by a second reaction for the qPCR amplification of the gene of interest. The one-step reaction is more suited for high-throughput screening when sample availability is unlimited. The two- step format allows for the amplification of multiple genes when the quantity of

RNA template available is limited, the capability for more extensive optimisation and the ability to archive the 1st strand of cDNA for future analysis[297].

5.1.4 Priming consideration

Primers are short DNA sequences complementary to the target region that selectively amplifies the target region along with DNA polymerase. Priming strategies for the reverse transcription reaction fall into the following categories: Oligo (dT), random and gene-specific[298].

i) Oligo (dT) priming Oligo (dT) primers are oligonucleotides comprised of thymine bases. They are specific for mRNA as the latter has a polyA tail (adenine binds to thymine). Oligo (dT) priming achieves an accurate cDNA representation of the mRNA fraction. This method requires high quality RNA that is full-length. It is not a good choice to prime for RNA that is likely to be fragmented[291].

ii) Random priming Random primers are usually hexamers or nonamers with a random combination of A, T, G and C bases. This method yields the largest amount of cDNA as the primers can reverse transcribe the majority of the total RNA (i.e. ribosomal RNA, messenger RNA and transfer RNA). It is the least satisfactory method of synthesising cDNA as the RT reaction is not focused to the mRNA fraction, which is the coding region of the gene[291].

iii) Gene-specific priming Gene–specific primers are designed by the researcher to specifically target the transcript of interest and thus provide the most sensitive method of quantification. However, they require separate priming reaction for each

target and therefore are not practical where the amounts of RNA available are limited[291].

5.1.5 qRT - PCR chemistry options

Two different methods are currently used to detect the amplification products of the qRT-PCR experiment.[299]

1. A sequence specific probe which consists of an oligonucleotide labelled with a fluorescent dye and a quencher (e.g. Taqman probes, Molecular Beacons and Scorpions).
2. A non-specific DNA binding dye such as SYBR Green I that fluoresce when bound to double-stranded DNA.

5.1.5.1 Probe-based chemistries

An internal probe is used to detect the qPCR product of interest and therefore increases detection specificity. The probe is bound to a reporter dye and a quencher. In the absence of a specific target, the probe remains quenched. Conversely, in the presence of a specific target, the probe fluoresces. The level of fluorescence correlates with the amount of amplified targets[299;300].

i) Hydrolysis probes Linear or Taqman probes are oligonucleotides with a fluorescent reporter dye, typically 6–carboxyfluorescin (FAM) attached at the 5' end of the probe and a quencher such as tetramethylrhodamine (TAMRA) attached at the 3' end of the probe[300]. As long as the reporter and the quencher are within close

proximity, no fluorescence is detected. The probe is designed to anneal to one strand of the target sequence just slightly downstream of one of the primers. As the polymerase extends that primer, it encounters the 5’ end of the probe. Taq DNA polymerase has 5’-3’ nuclease activity so that it displaces and degrades the 5’ end, releasing free reporter dye into the solution. Fluorescence can be detected following separation of the reporter dye and the quencher. The different steps are illustrated in Figure 5.1. The main advantages of hydrolysis probes are that they are specific and can be multiplexed (simultaneously measures multiple analyses using a single assay). They are however costly.

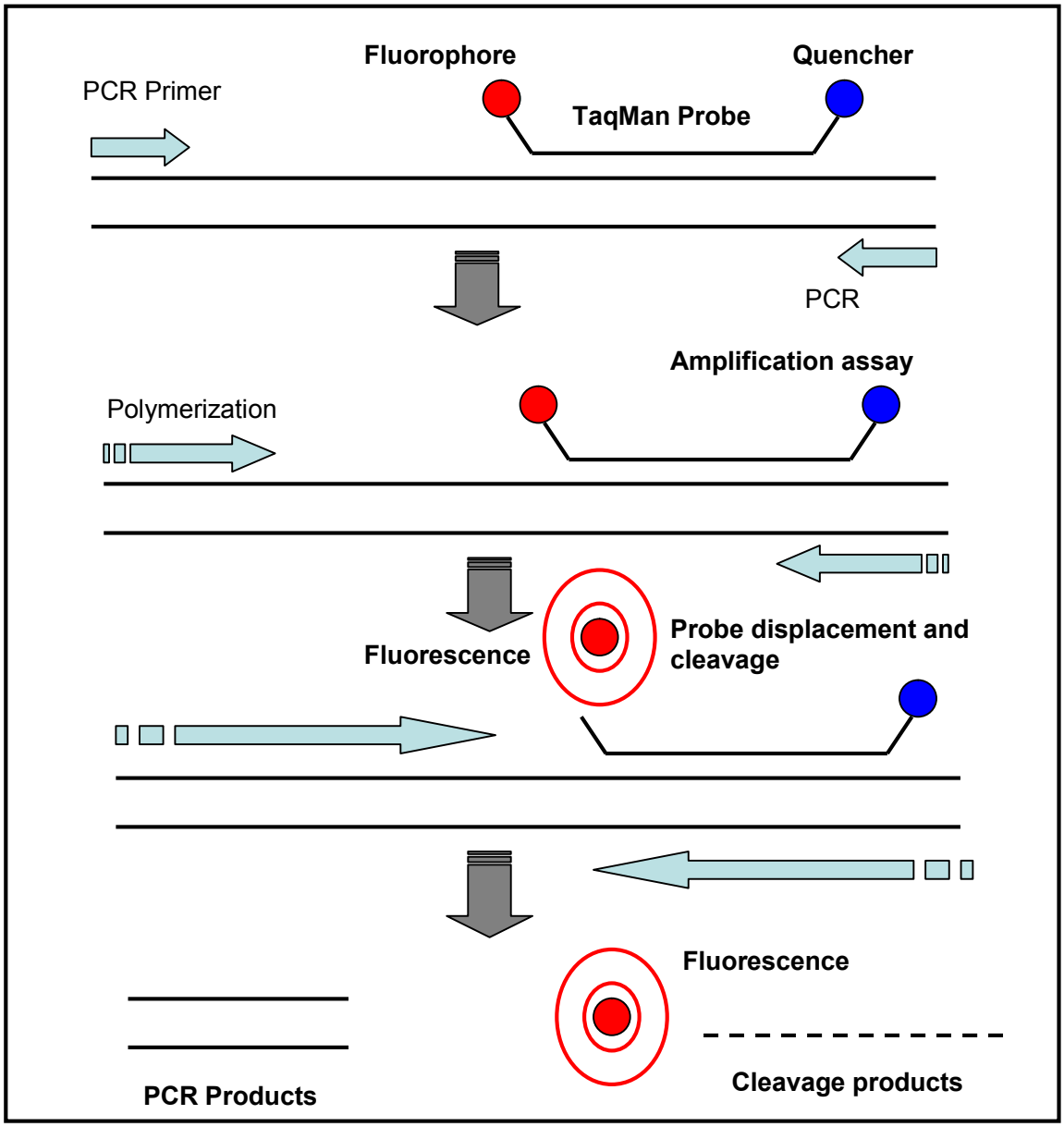


Figure 5.1 Taqman probe chemistry mechanism.

ii) Hybridisation probes Molecular Beacons consist of a hairpin loop structure[300]. The central loop sequence is complimentary to the target of interest and the stem arms are complementary to each other. One end of the stems has a reporter fluorophore while the other end carries a quencher. Since they are in close proximity, no fluorescence is produced. In the presence of a target sequence, the annealing of

the loop sequence to the target causes the separation of the fluorophore and the quencher thus allowing detection of the reporter sequence. The different steps are illustrated in Figure 5.2. Hybridisation probes are specific, can be multiplexed and their reactions are reversible. They are however difficult to design.

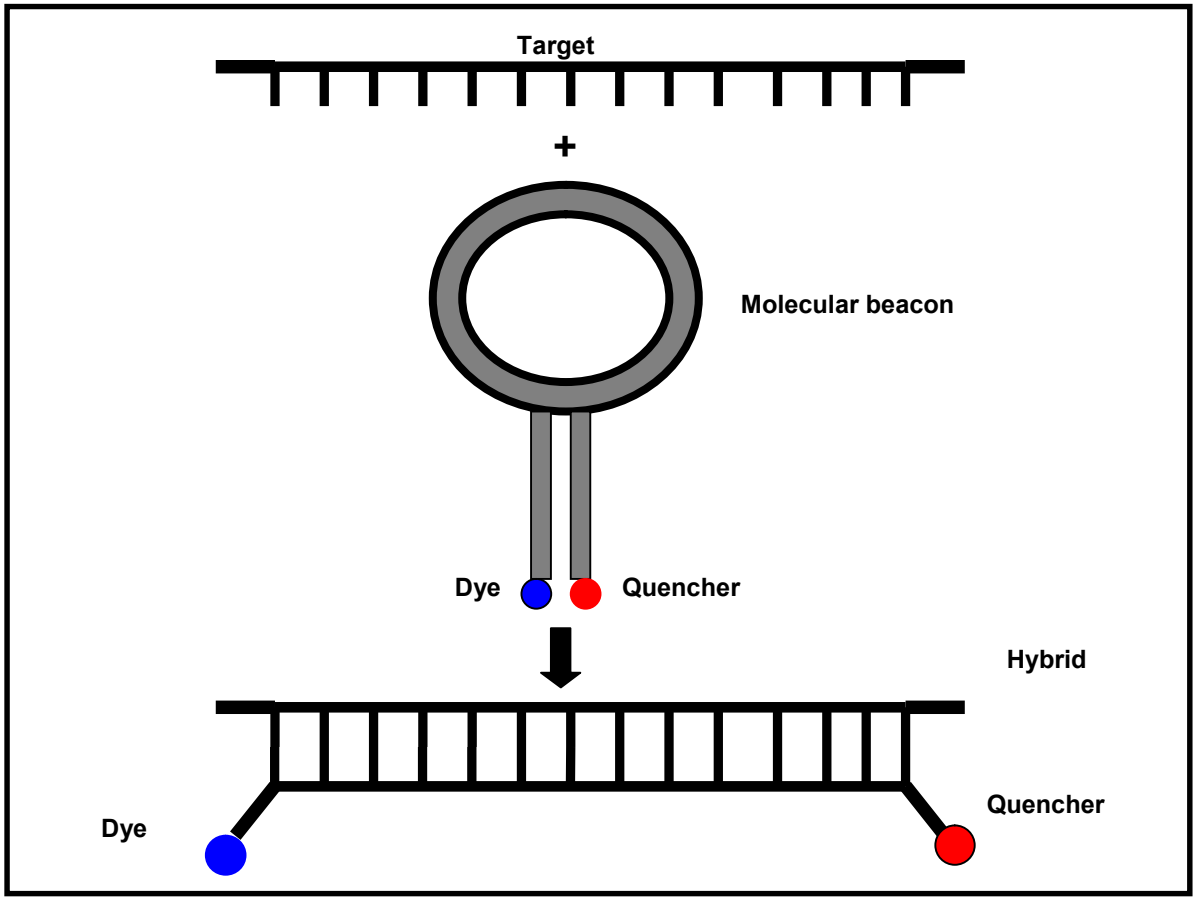


Figure 5.2 Molecular beacon chemistry. When the target anneals to the molecular beacon, a hybrid is formed with separation of the fluorophore and quencher allowing fluorescence to be detected.

5.1.5.2 DNA Binding Dyes

SYBR Green I displays relatively low fluorescence when free in solution, but in the presence of double-stranded DNA, its fluorescence increases by 1000-fold and in proportion to the DNA concentration of the sample (Figure 5.3). Detection of the target is therefore amplified. The concentration of double stranded DNA can be directly measured by the increase in fluorescence signal. The advantages of SYBR Green I are its relatively low cost and the assays are relatively easy to design and run. However, the main limitation is its non–specificity as SYBR Green will bind to any double-stranded DNA. Non-specific binding can be avoided by designing specific primers[299;300].

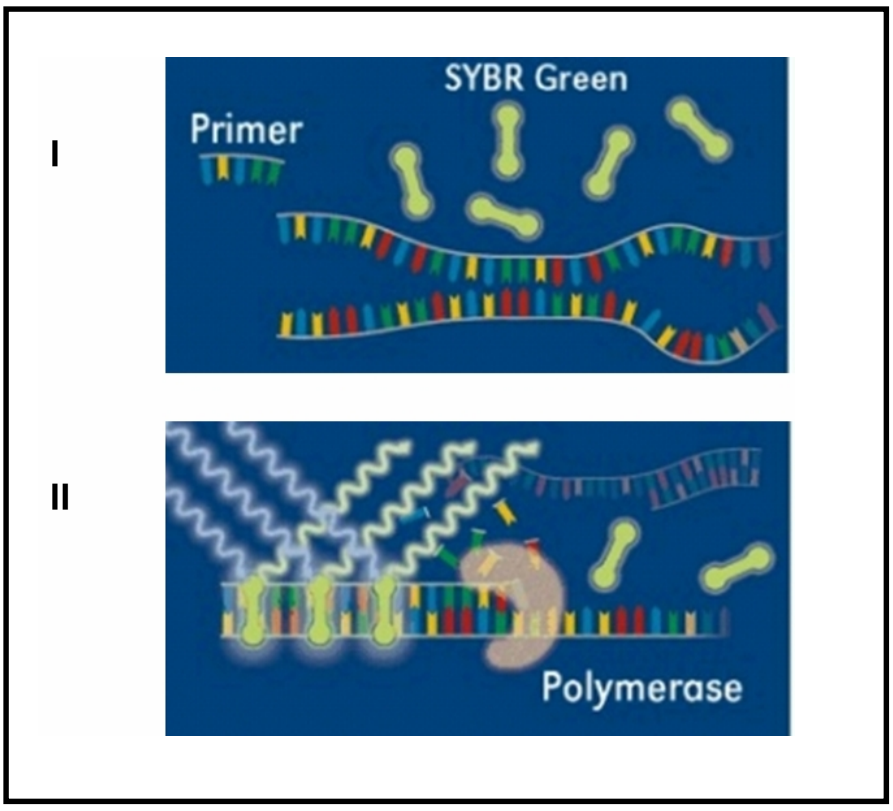


Figure 5.3 SYBR Green I detection mechanism. In the bound state SYBR Green is 1000-fold more fluorescent than in the unbound state.

5.1.6 Real time amplification and analysis

Following the RT steps and choice of appropriate detection chemistry, a detection system such as the ABI Prism 7000 Sequence Detection Systems (Applied Biosystems) is used to report on the presence of PCR products. It monitors the amplification in real-time and provides appropriate software for quantitative analysis. In essence, qRT-PCR is characterised by the point in time during cycling when amplification of a PCR product is first detected. Conventionally, traditional PCR detects PCR products at the endpoint of the reaction. However; there is considerable variability in the endpoints between replicates making these results unreliable[291;300].

Figure 5.4 shows examples of the amplification plots for 3 samples. The C_t values represent the cycle fractions where the instrument can first reliably detect fluorescence derived from the amplification reaction. The higher the starting copy number of the nucleic acids, the sooner a significant increase in fluorescence is noted and the smaller the C_t value.

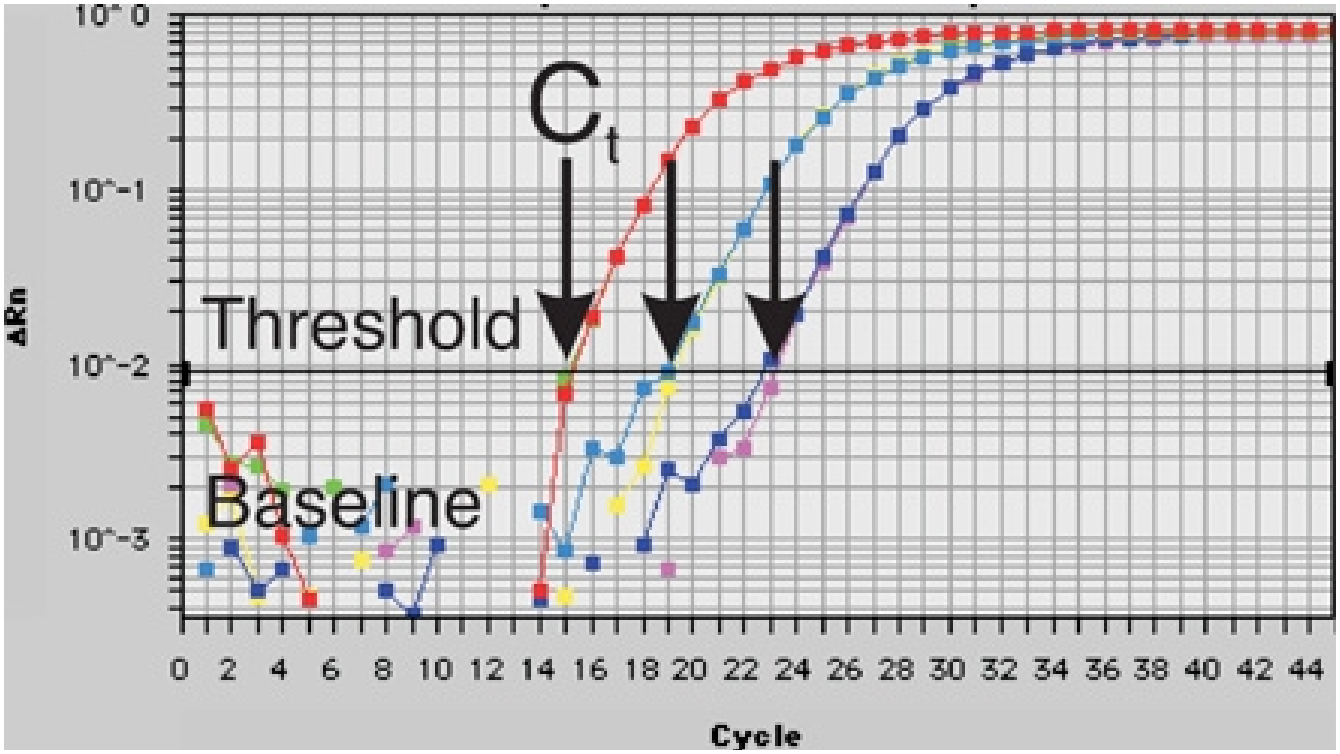


Figure 5.4 qRT-PCR amplification plots of fluorescence signal versus cycle number[301].

5.2 Methods

5.2.1 Experimental design

A relative quantification method was used for the purpose of this experiment with RNA from NA as the calibrator. RNA was extracted from AAA wall (n=13), AOD wall (n=10) and NA wall (n=7) using the method described in section 2.2.

The number of genes that could be confirmed in this experiment were limited both by the amount of RNA available and cost. Nine genes were thus chosen for confirmation by qRT-PCR. MMP-3, MMP-9 and Cathepsin H were included as positive controls for the experiment as these genes have been confirmed in previous studies carried out at our laboratory[67;123]. The expressions of these genes have also been inconsistent in different studies involving AAA. Novel genes were included based on a literature review and their likelihood of affecting AAA development based on what is already known regarding their biological functions. CD79A and Spi-B transcription factor are located on chromosome 19q13, a susceptible locus for AAA. CD19 is a marker of B-cells and the majority of the differentially expressed inflammatory genes with the highest fold change in the microarray experiment were related to B-cells.Thus, by confirming CD19, the top genes in the experiment will be confirmed. SPEG and BMP-6 have not been studied in AAA development but as explained in Chapter 7, they may influence AAA formation. ADAMTS-9 was also included as a novel gene due to its ability to break down the extracellular matrix.

A two-step RT reaction was carried out using Taqman probes and assays (designed by Applied Biosystems). Only exon spanning probes (Table 5.2) were chosen as they do not anneal with genomic DNA and therefore decrease the frequencies of non-specific binding.

Table 5.2: Primers used for the RT-PCR step (Applied Biosystems).

Taqman Gene Expression Assays	Gene Name
Hs00172025_m1	A disintegrin and metalloproteinase with thrombospodin motif-9
Hs01099594_m1	Bone morphogenic protein 6
Hs00544778_m1	Cathepsin H
Hs99999192_m1	CD19
Hs00233566_m1	CD79A
Hs00233962_m1	Matrix metalloproteinase 3
Hs00957562_m1	Matrix metalloproteinase 9
Hs00162150_m1	Spi-B transcription factor
Hs00195347_m1	SPEG complex locus

5.2.2 Reverse transcription (RT)

The Enhanced Avian RT First Strand Synthesis Kit (Sigma, USA) was used for the RT reaction. Total RNA (1.5µg) was used as a starting template for the reaction. The total RNA was mixed with 1µl of oligo $(dT)_{23}$ primer and 1µl of dNTP to a final volume of 10µl in a PCR microcentrifuge tube (Eppendorf, UK) on ice. The tube was then incubated for 10 minutes at 70°C in a thermal cycler. The following components were then added as shown in the Table 5.3 below:

Table 5.3 RT step reagents.

Reagent	**Volume (µl)**
10 × buffer for eAMV-RT	2
Enhanced avian RT	1
RNase inhibitor	1
RNAse free water	6
Total volume	20

The tube was incubated at 50°C for 50 minutes. The first strand cDNA was ready for subsequent amplification.

5.2.3 qPCR Step

Target amplification was carried out using TaqMan Gene Expression Assays (Applied Biosystems) according to their recommended protocol. The PCR reaction was carried out in a 96–well plate (Applied Biosystems). Each reaction was carried out in triplicate for both the gene of interest and the housekeeping genes, GAPDH (Applied Biosystems) and β-actin (Applied Biosystems). Expressions of the housekeeping genes have been shown to be constant in previous work carried out on vascular tissue in our laboratory[258] (Section 5.1.3). A standard which is a 1:100 dilution of all the samples in the experiment was used on each plate to correct for variability in the efficiency of the PCR machine between plates. A 'no template control' (i.e. RNAse free water) was also used on each plate to rule out cross-contamination of reagents and surfaces. The reaction size in each well was 25µl and consisted of reagents as shown in Table 5.4. Each plate was set up as in Figure 5.5.

Table 5.4 qPCR step reagents.

Component	**Volume (µl)**
Taqman Gene Expression Assay (20×)	1.25
cDNA template + RNAse free water	11.25
TaqMan Universal PCR Master Mix (2×)	12.5
Total Volume	25

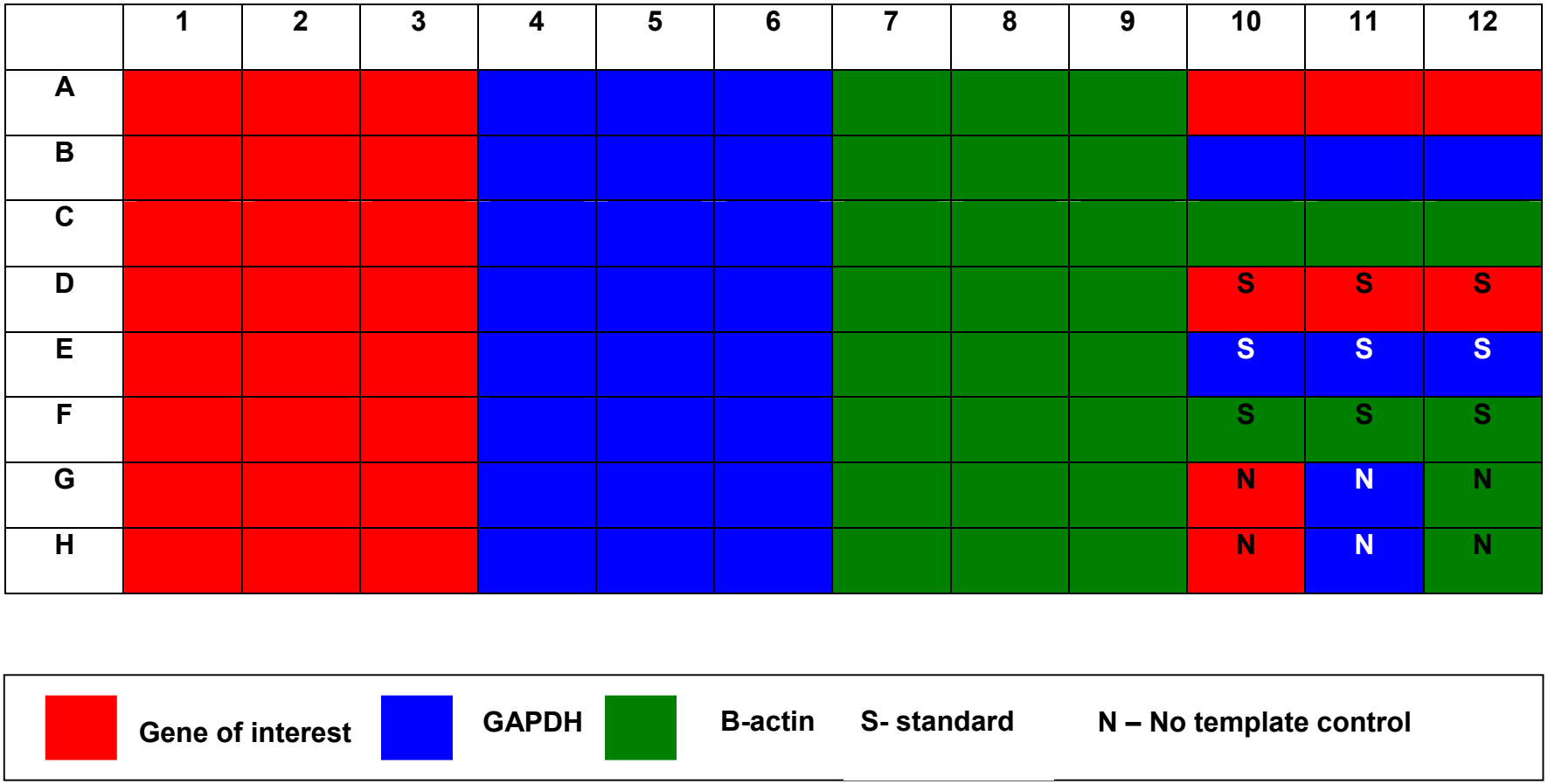


Figure 5.5 Plate set-up for each run on the ABI Prism 7000

The plate was covered with an optical adhesive cover and centrifuged for 1 minute to collect the reaction at the bottom of each well. Each plate was placed in the ABI 7000 Sequence Detection Systems (Applied Biosystems) using the recommended thermal cycling conditions (Figure 5.6).

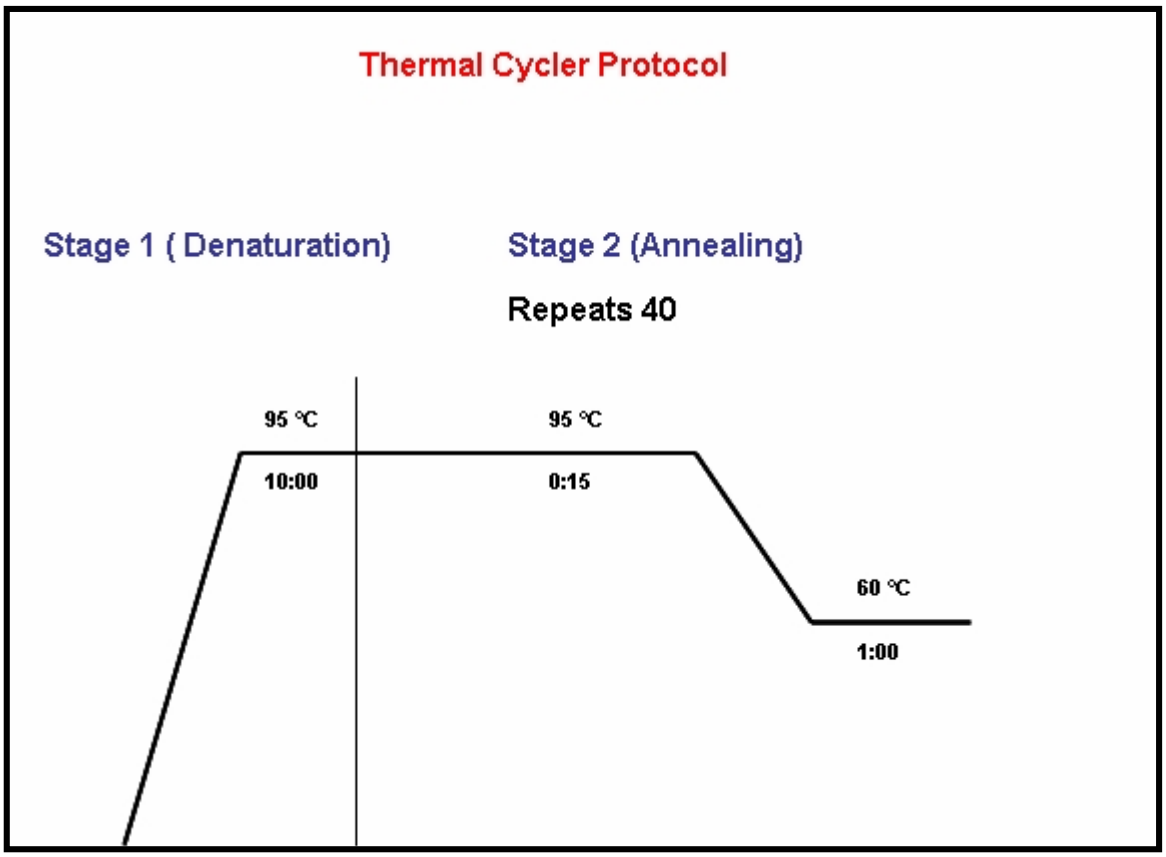


Figure 5.6 Thermal cycling profile.

5.2.4 Statistical analysis of qRT-PCR data

Relative gene expression was analysed using the $2^{-\Delta\Delta C}{}_t$ method [302] .The following equation was used to calculate $\Delta\Delta C_t$:

$$\mathbf{\Delta\Delta C_t = (\Delta C_t \text{ sample} - \Delta C_t \text{ housekeeping genes})}$$

ΔC_t sample = Average of ΔC_t values for the triplicates used for each sample

ΔC_t housekeeping genes = Mean of the ΔC_t values for GAPDH and B-actin

Fold change is derived from $2^{-\Delta\Delta C}{}_t$. Statistical differences in gene expression between AAA and AOD and AAA and NA were analysed by unpaired t test as the data was normally distributed and sample size in each group is unequal.

5.3 Results

Patient demographics for the samples used in the qRT-PCR experiment are shown in Table 5.5.

Table 5.5 Demographics of patients used in qRT-PCR experiment.

Demographics	AAA (n=13)	AOD (n=10)	NA (n=7)
Mean age	70 (61-80)	66 (53-66)	59 (50-67)
Median AAA size	6.6 (5.3-9.0)	----	----
Sex (M / F)	10 / 3	8 / 2	6 /1
Smoking	9	8	5
Hypertension	8	4	4
IHD	7	8	0
Diabetes	4	3	1

There was no significant difference between the AAA and AOD groups of patients in terms of the demographic variables listed in Table 5.5. As expected, patients in the NA group were younger and had a healthier profile in terms of their cardiovascular risk factors.

The RNA samples used were all of high qualities with RIN > 5.5 as shown in Table 5.6 A, B and C below.

Table 5.6A Quality of aneurysm samples used.

AAA samples	RIN	A 260/280 ratio
AAA1	8.5	2.1
AAA2	7.5	2.1
AAA3	7.6	2.1
AAA4	7.3	2.1
AAA5	7.5	2.0
AAA6	7.5	1.9
AAA7	6.2	2.1
AAA8	7.1	1.9
AAA9	6.6	1.9
AAA10	6.4	1.9
AAA11	7.0	2.0
AAA12	7.1	2.0
AAA13	7.2	2.0

Table 5.6B Quality of AOD samples used.

AOD samples	RIN	A 260/280 ratio
AOD1	6.7	2.1
AOD2	7.2	2.1
AOD3	6.8	2.1
AOD4	6.9	2.1
AOD5	6.1	1.9
AOD6	6.1	2.0
AOD7	6.2	2.0
AOD8	6.2	2.1
AOD9	5.7	2.0
AOD10	6.2	2.0

Table 5.6C Quality of NA samples used.

NA samples	RIN	A260/280 ratio
NA1	6.7	2.0
NA2	7.0	2.0
NA3	6.2	2.1
NA4	6.5	2.0
NA5	6.3	2.0
NA6	6.5	2.0
NA7	6.2	2.0

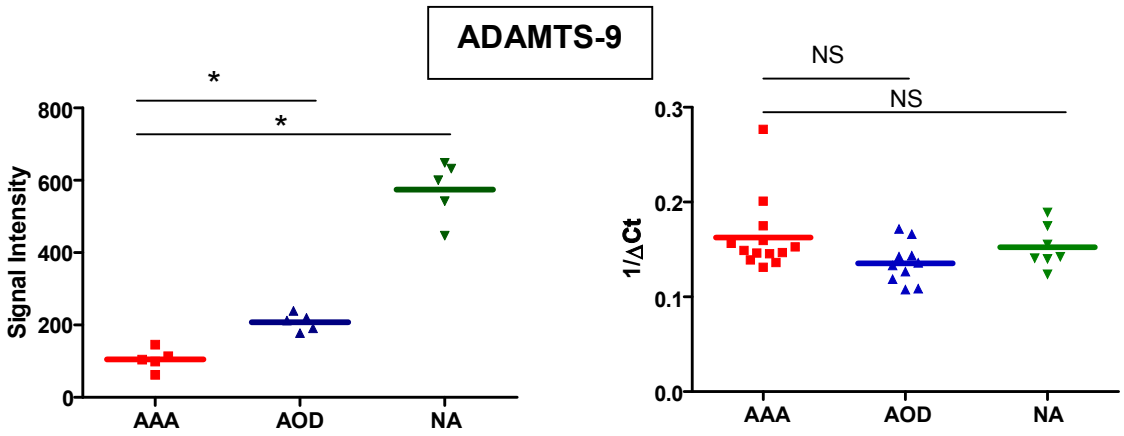
Patterns of mRNA expression for a selection of 9 genes were independently examined using qRT-PCR. Raw data for each gene is shown in Appendix O. The results for fold change and significance for each gene of interest are shown in Table 5.7(AAA vs. AOD) and Table 5.8(AAA vs. NA). The results for the qRT-PCR and the microarray experiment are represented graphically for each gene (Figure 5.7).

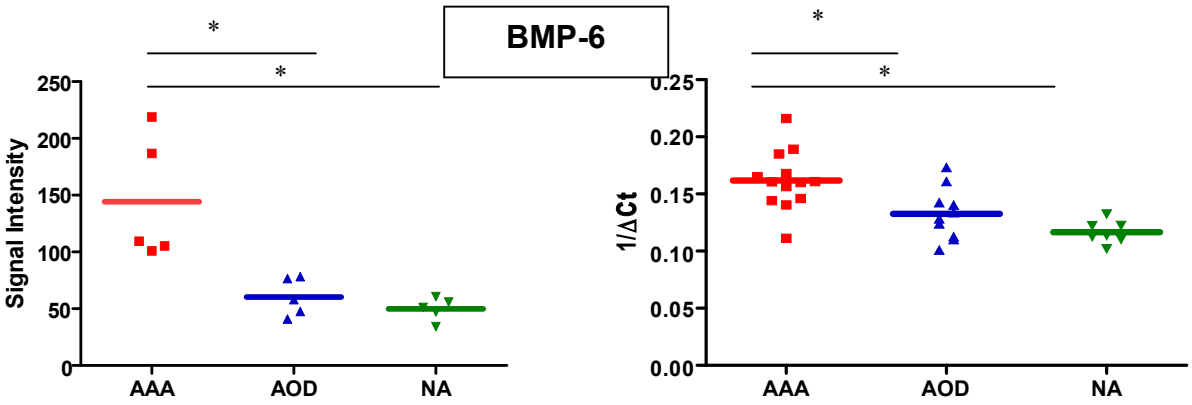
Table 5.7 Relative quantification of mRNA expression between AAA and AOD using qRT-PCR. SPEG is downregulated.

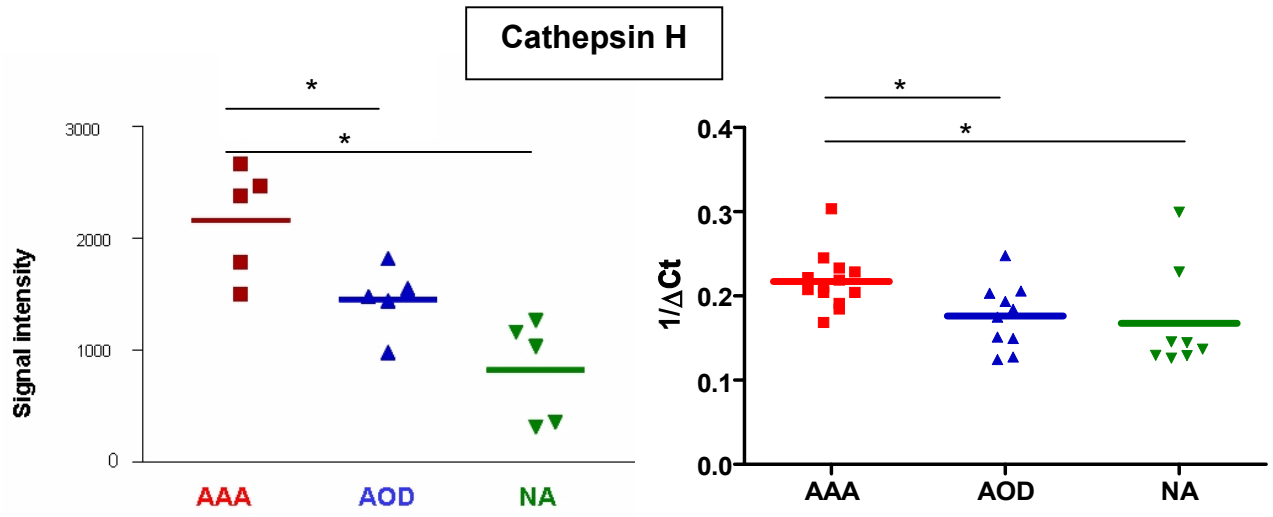
Gene Symbol	AAA (ΔΔ C_T) (n=13) (mean ± SD)	AOD (ΔΔC_T) (n=10) (mean ± SD)	Fold Change	P value
ADAMTS9	6.382 ± 1.080	7.554 ± 1.188	2	0.025
BMP-6	6.589 ± 1.390	7.743 ± 1.708	2	0.042
CATH	4.697 ± 0.652	5.929 ± 1.321	2	0.009
CD19	6.619 ± 1.934	10.975 ± 4.342	20	0.002
CD79A	3.754 ± 1.667	6.835 ± 3.435	6	0.010
MMP-3	10.459 ± 2.217	14.872 ± 5.137	21	0.010
MMP-9	4.178 ± 3.521	3.990 ± 2.476	0.9	0.441
SPIB	7.415 ± 2.023	11.222 ± 4.601	14	0.015
SPEG	8.521 ± 1.169	7.185 ± 1.738	0.3	0.027

Table 5.8 Relative quantification of mRNA expression between AAA and NA using QRT-PCR. SPEG is downregulated.

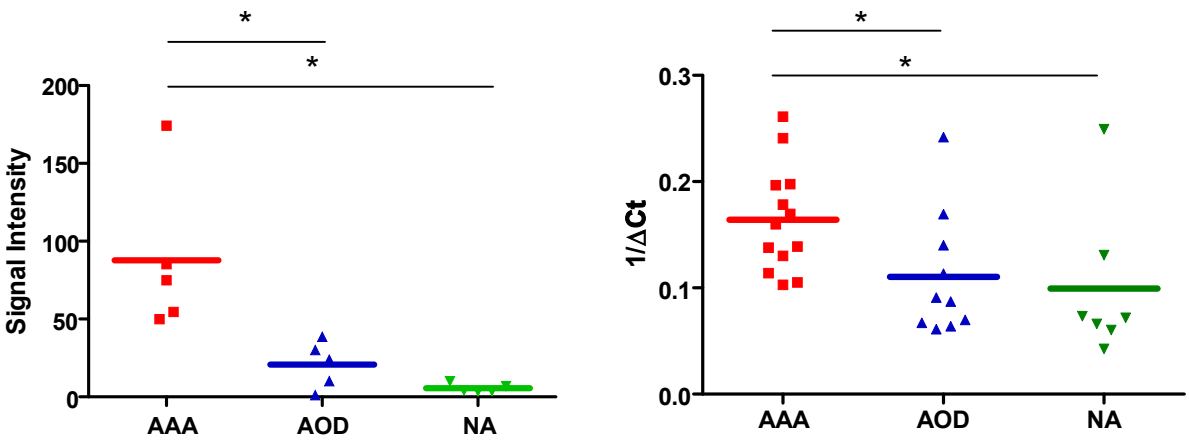
Gene Symbol	AAA ($\Delta\Delta C_T$) (n=13) (mean ± SD)	NA ($\Delta\Delta C_T$) (n=7) (mean ± SD)	Fold Change	P value
ADAMTS9	6.382 ± 1.080	6.777 ±0.916	1.7	0.191
BMP-6	6.589 ± 1.390	8.734±0.735	4	<0.001
CATH	4.697 ± 0.652	6.527±1.713	4	0.010
CD19	6.619 ± 1.934	14.001±5.983	167	0.004
CD79A	3.754 ± 1.667	9.308±3.782	47	0.002
MMP-3	10.459 ± 2.217	15.750±3.561	39	0.002
MMP-9	4.178 ± 3.521	6.457±3.284	5	0.040
SPIB	7.415 ± 2.023	12.766±3.81	40	0.009
SPEG	8.521 ± 1.169	6.433±0.440	0.25	<0.001


ADAMTS-9
Signal Intensity
800
600
400
200
0
AAA
AOD
NA
*
*
1/ΔCt
0.3
0.2
0.1
0.0
NS
NS

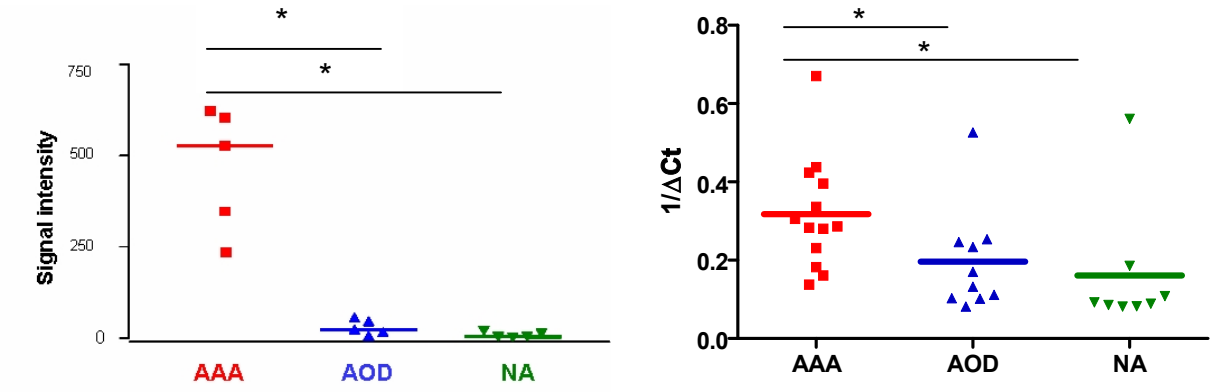

BMP-6
Signal Intensity
250
200
150
100
50
0
AAA
AOD
NA
*
*
1/ΔCt
0.25
0.20
0.15
0.10
0.05
0.00


Cathepsin H
Signal intensity
3000
2000
1000
0
AAA
AOD
NA
*
*
1/ΔCt
0.4
0.3
0.2
0.1
0.0

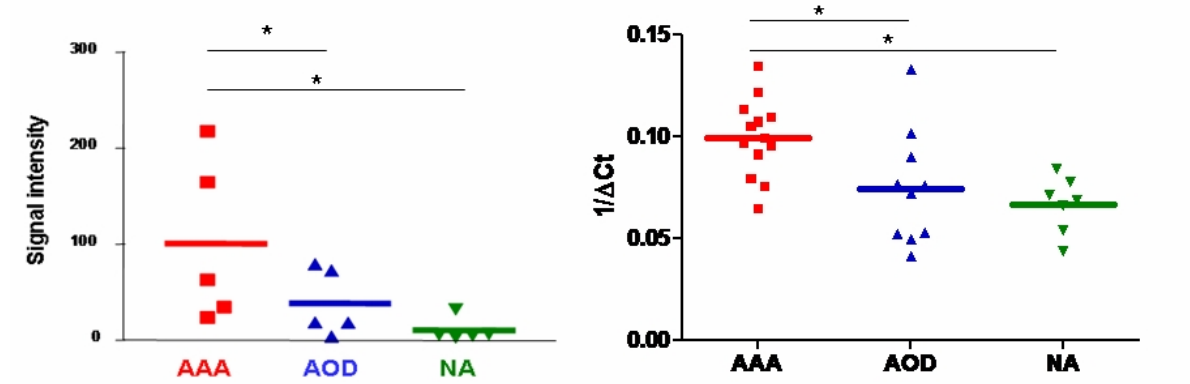
CD19



CD79A



MMP-3



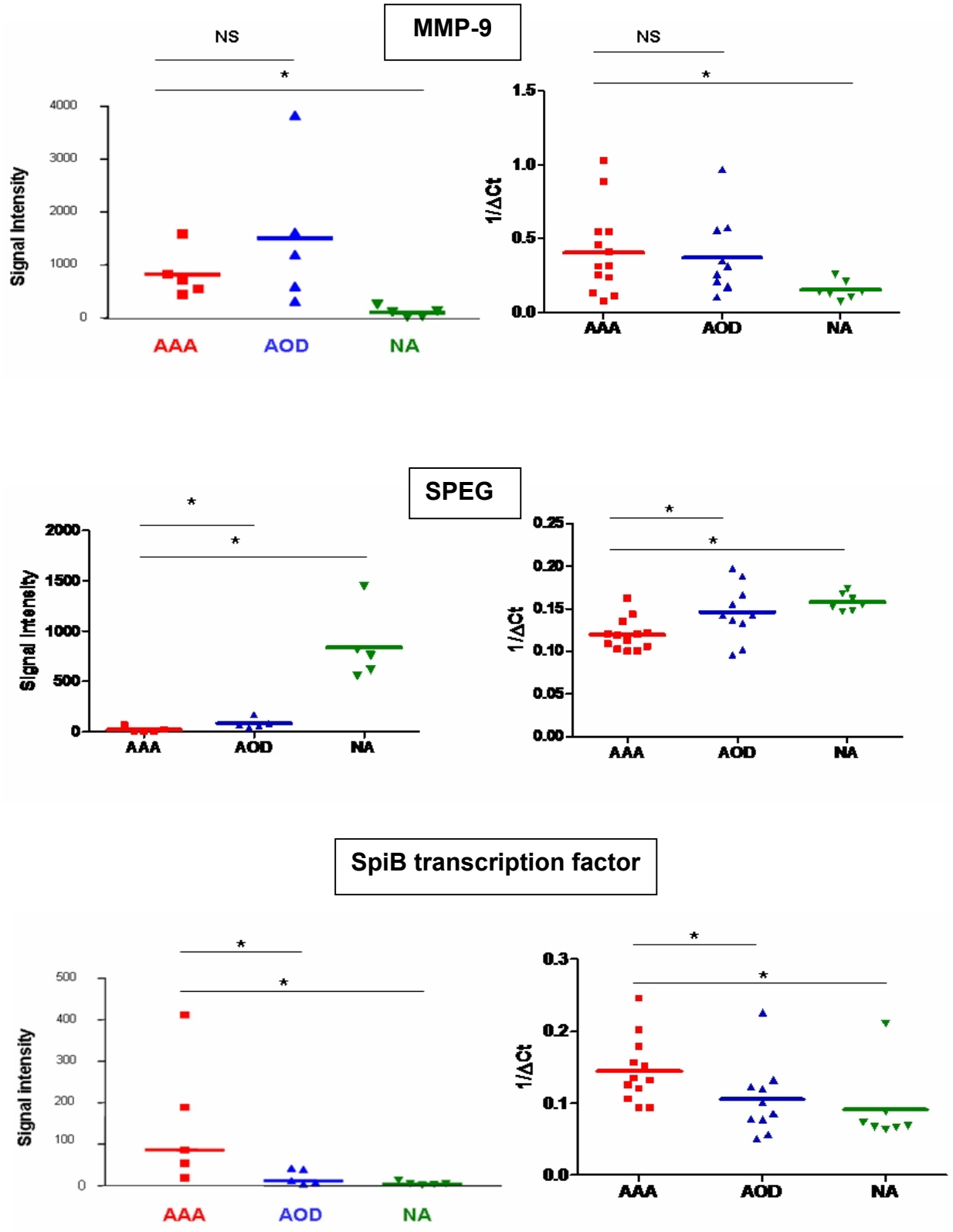


Figure 5.7 Graphical representations of microarray and qRT-PCR data for each gene. NS- not significant and * P < 0.05.

5.4 Discussion

The qRT-PCR experiment confirmed the microarray results on a larger sample size for each of the genes probed except for ADAMTS-9 when comparing AAA with NA. These results add to the robustness of the microarray data. The sequences used for genes in the PCR experiment were different to that on the microarray platform and this might account for the differing result for ADAMTS-9. This high confirmatory rate (8 out of 9 genes confirmed) is similar to that reported by other microarray studies[95;258].

The sample sizes for AOD and NA were limited by availability of samples. Only a few AOD samples were available as angioplasty has superseded aortic bypass surgery in the treatment of aortic occlusive disease. It is not feasible to obtain tissue during angioplasty. This also limited the total number of genes that could be confirmed as only limited quantities of total RNA could be extracted from the available samples.

Chapter 6

Biostatistical analysis: pathways and networks.

6.1 Introduction

The identification of the most differentially expressed genes in any dataset is clearly a valid approach. Pathway and network analysis can, however, also be used to identify potentially smaller, but consistent changes in expression of a group of genes with related functions. The aim of this analysis was to identify pathways and/or networks that were significantly enriched and may therefore be involved in the pathogenesis of AAA.

Enrichment analysis is used to determine the most populated pathways or networks for a particular set of differentially expressed genes.

i) Pathway analysis. This analysis can be applied to maps which contain information of the type that might be found in a text book or review article (canonical). A pathway has a defined start and end, usually spanning from the extracellular space, through ligands and receptors, to intracellular signalling via enzymes and kinases to nuclear functions mediated by transcription factors.

ii) Network analysis. Unlike pathway maps (canonical), networks can be composed of 1-step associations and may or may not be part of an established pathway. An algorithm intended to find regulatory pathways that are activated under pathological conditions can also be used. It defines a set of transcription factors that are directly regulating genes of interest and a set of receptors whose ligands are in the list of interest and then constructs series of networks. Each network contains all shortest paths from a receptor to the selected transcriptional factors and their targets. This

approach allows us to reveal the most important areas of regulatory machinery affected under the investigated pathological condition.

Affected networks were identified using the Z score which is based on the number of fragments of canonical pathways present and are sorted by enrichment p-value.

$$z-score = \frac{r - n\frac{R}{N}}{\sqrt{n\left(\frac{R}{N}\right)\left(1-\frac{R}{N}\right)\left(1-\frac{n-1}{N-1}\right)}} = \frac{r-\mu}{\sigma}$$

r – number of interactions the objects has with objects in the active experiment

R – total number of network objects that interact with the object

n – number of network objects in the active experiment

N – total number of network objects in the database.

6.2 Methods

Differentially expressed gene lists were generated as previously described in (Sections 4.2.3 and 4.2.4) from the comparison of both AOD and AAA to normal artery. Those genes which were more than two fold upregulated with a p value of less than 0.05 were submitted for pathway analysis and network analysis. Legends to pathways and networks are shown in Appendix N.

All pathway and network analysis were conducted using MetaCore software Version 6.3 (GeneGo, Inc). A list of genes that was unique to AAA was generated. Enrichment analysis was used to determine the most populated pathways or networks for the set of differentially expressed genes which were unique to AAA. The likelihood that differentially regulated genes in the experimental dataset participate in a given pathway by chance was measured using the hypergeometric mean calculation and a p value was assigned.

Transcription factors and receptors involved in the different networks were identified. A transcription factor binds DNA and initiates a process of increased or decreased gene transcription. Thus, it regulates a number of important cellular processes including transcription regulation, differential enhancement of transcription, cell differentiation and response to intercellular signals[303]. Receptors are transmembrane or intra-cellular proteins to which ligands (such as pharmaceutical agents) bind resulting in a cellular response. These molecules are important as they are putative pharmacological tagets[303].

6.3 Results

There was approximately the same number of genes that were unique to AAA or AOD (Figure 6.1).

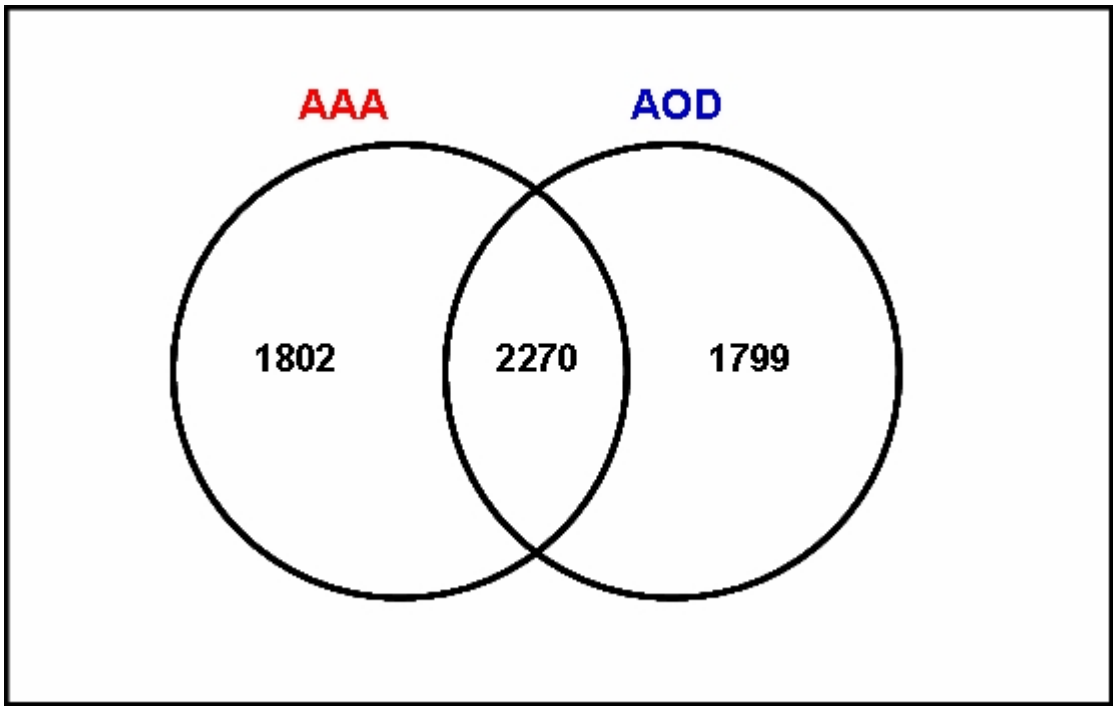


Figure 6.1 Venn diagram showing the number of unique genes for AAA and AOD.

6.3.1 Pathway analysis

Top pathway maps suggest immune and inflammatory themes with involvement of the complement pathway, CCR3 signalling and histamine signalling (Figure 6.2). The top 2 maps are detailed below (Figures 6.3 and 6.4).

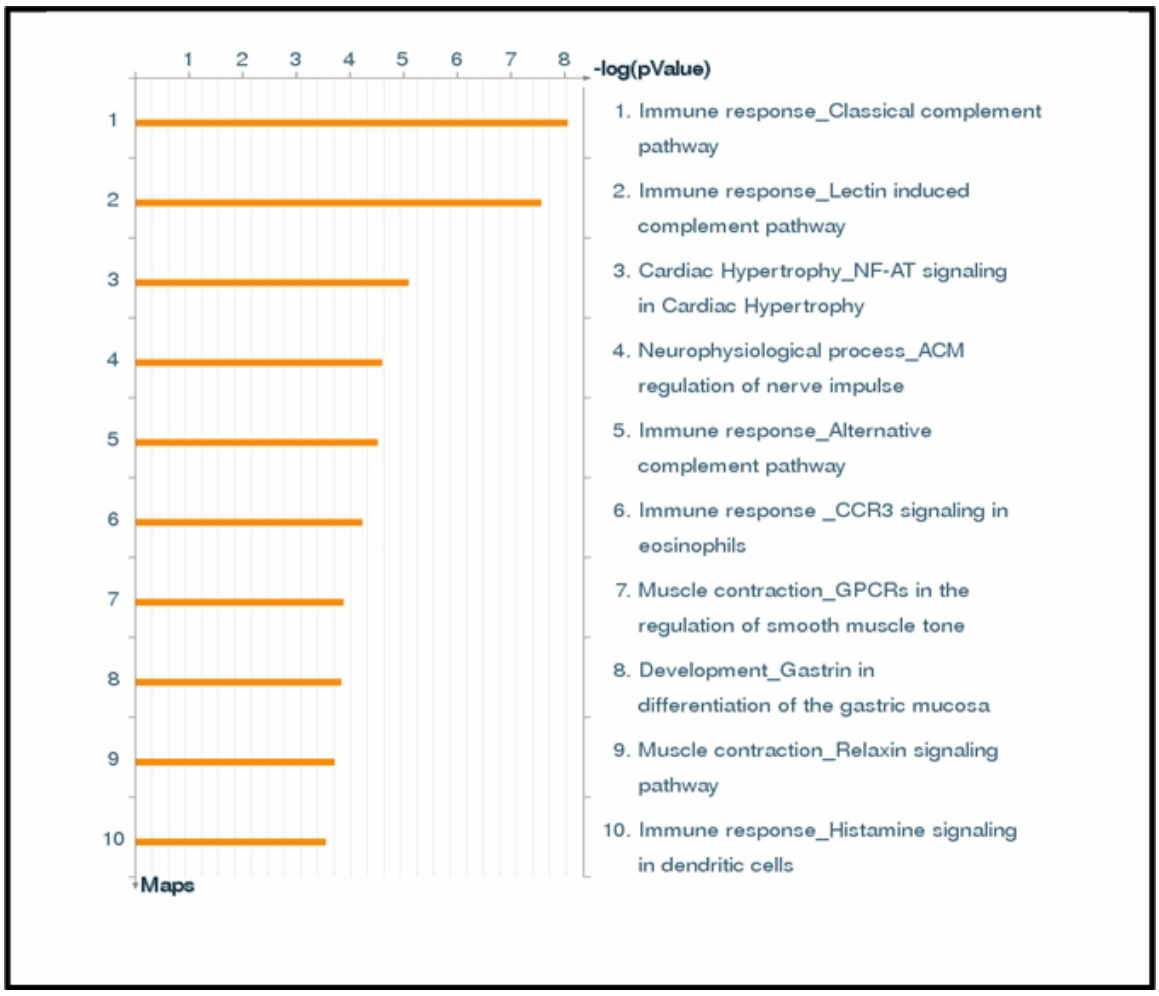


Figure 6.2 Main pathway maps involving differentially expressed genes associated with AAA.

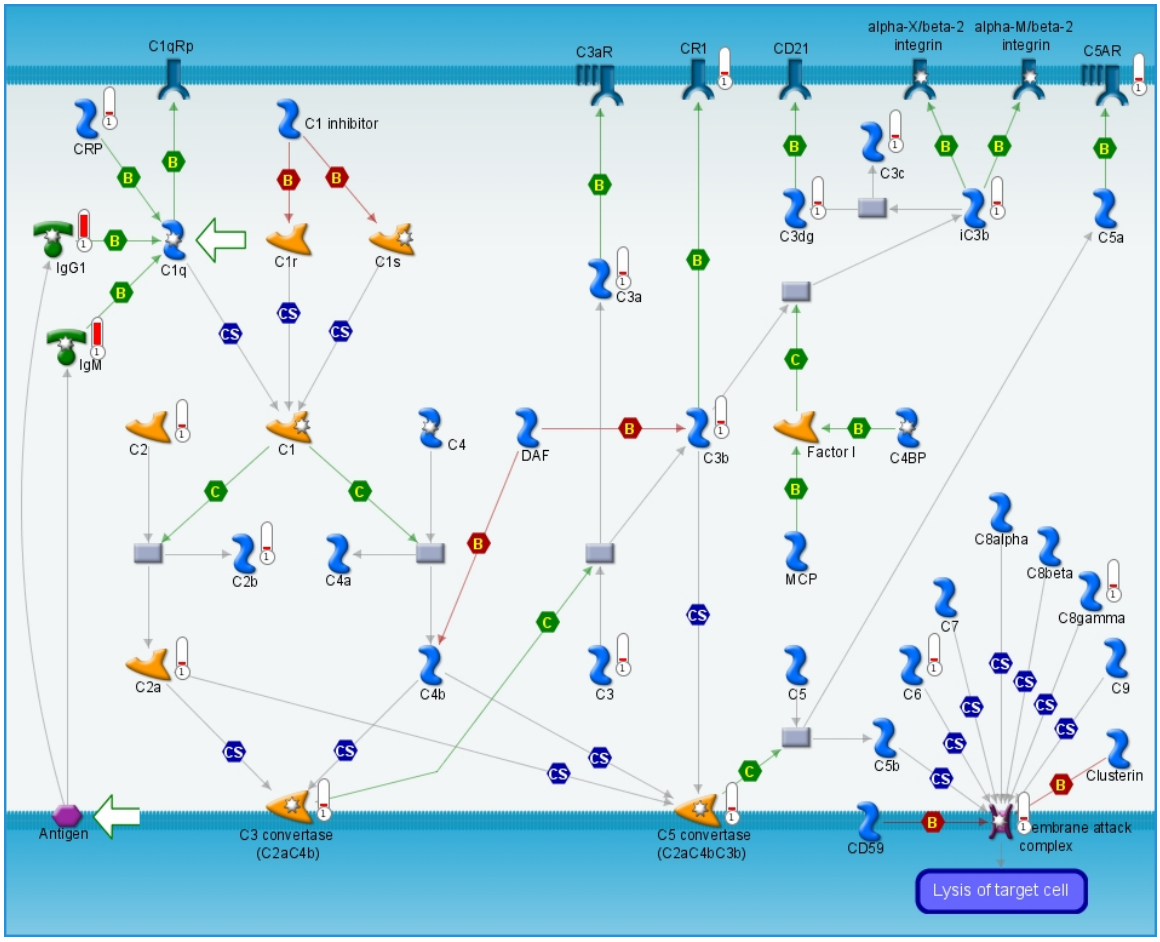


Figure 6.3 Immune response: Classical complement pathway.

Red thermometers show a gene that is upregulated. Green arrows represent positive, red negative and grey unspecified interactions. Boxes on the line represent the type of regulation: B = binding, C= cleavage and CS= complex subunit (Protein is a subunit of a protein complex).

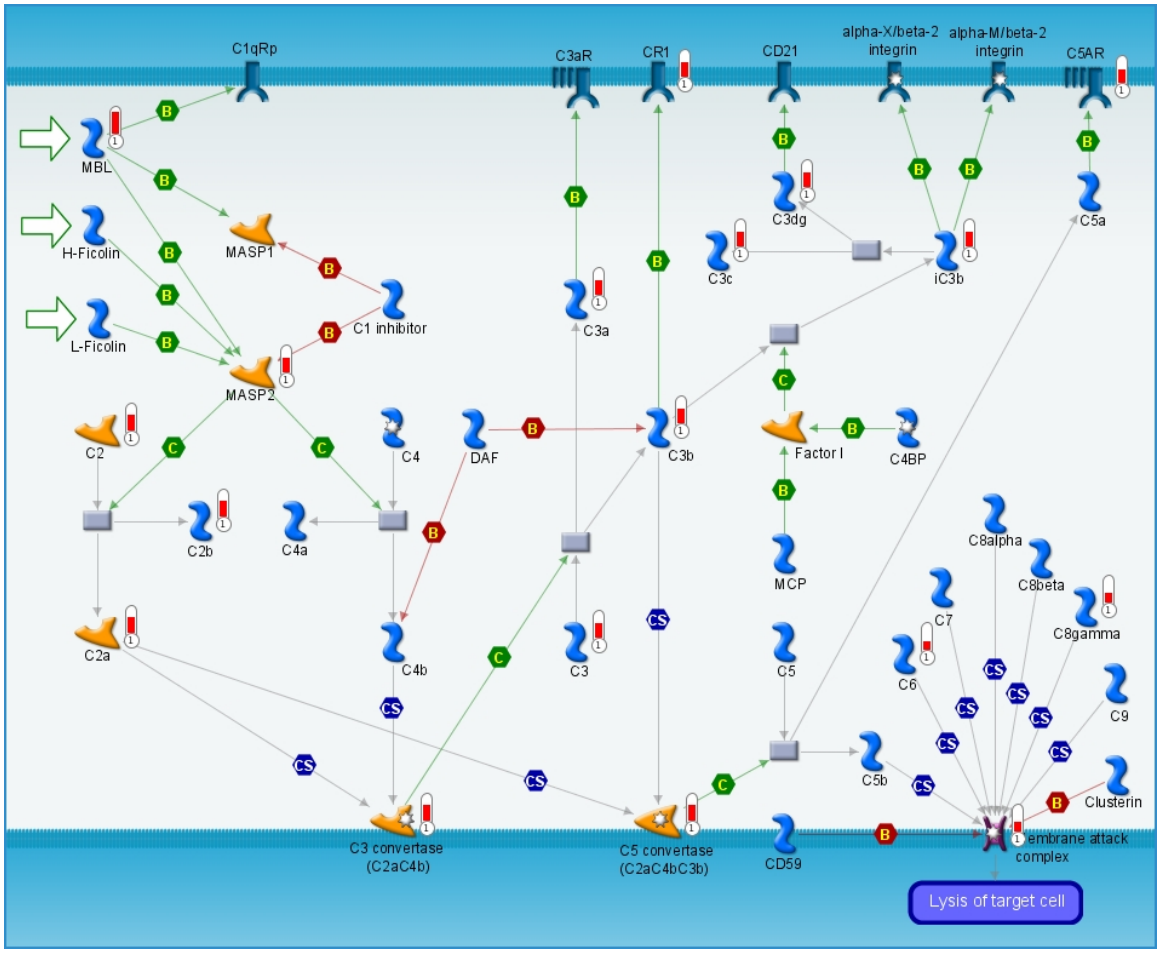


Figure 6.4 Immune response: lectin induced complement pathway.

Red thermometers show a gene that is upregulated. Green arrows represent positive, red negative and grey unspecified interactions. Boxes on the line represent the type of regulation: B = binding, C= cleavage and CS= complex subunit (Protein is a subunit of a protein complex).

A large number of upregulated genes in AAA compared with AOD were involved in both pathways. In the classical complement pathway, 17 out of 37 genes were significantly upregulated in AAA compared with AOD. There was no downregulated

gene. In the lectin induced complement pathway, 17 out of 41 genes were significantly upregulated in AAA compared with AOD.

6.3.2 Network analysis

The top five networks selected on the basis of the number of fragments of canonical pathways present and sorted by enrichment p-value (Table 6.1) are described below.

Table 6.1: Top five networks are detailed with respect to P-value, g Score and Z score

Network	GO Processes	Total nodes	Root nodes	Pathways	P-value	Z score	g score
1	Organ development (73.5%), positive regulation of transcription (51.0%), positive regulation of gene expression (51.0%)	50	19	101	1.02e-17	15.71	141.96
2	Regulation of cell proliferation (72.9%), response to organic substance (66.7%), positive regulation of biological process (81.2%)	50	14	71	2.47e-11	11.27	100.02
3	Response to steroid hormone stimulus (28.6%), response to hormone stimulus (32.7%), response to organic substance (40.8%)	52	22	34	9.38e-22	18.17	60.67
4	Positive regulation of transcription (41.7%), positive regulation of transcription, DNA-dependent (39.6%), positive regulation of macromolecule biosynthetic process (43.8%)	50	27	29	8.37e-30	22.81	59.06
5	Positive regulation of biological process (66.0%), response to organic substance (50.0%), positive regulation of cellular process (62.0%)	50	25	23	1.42e-26	21.04	49.79

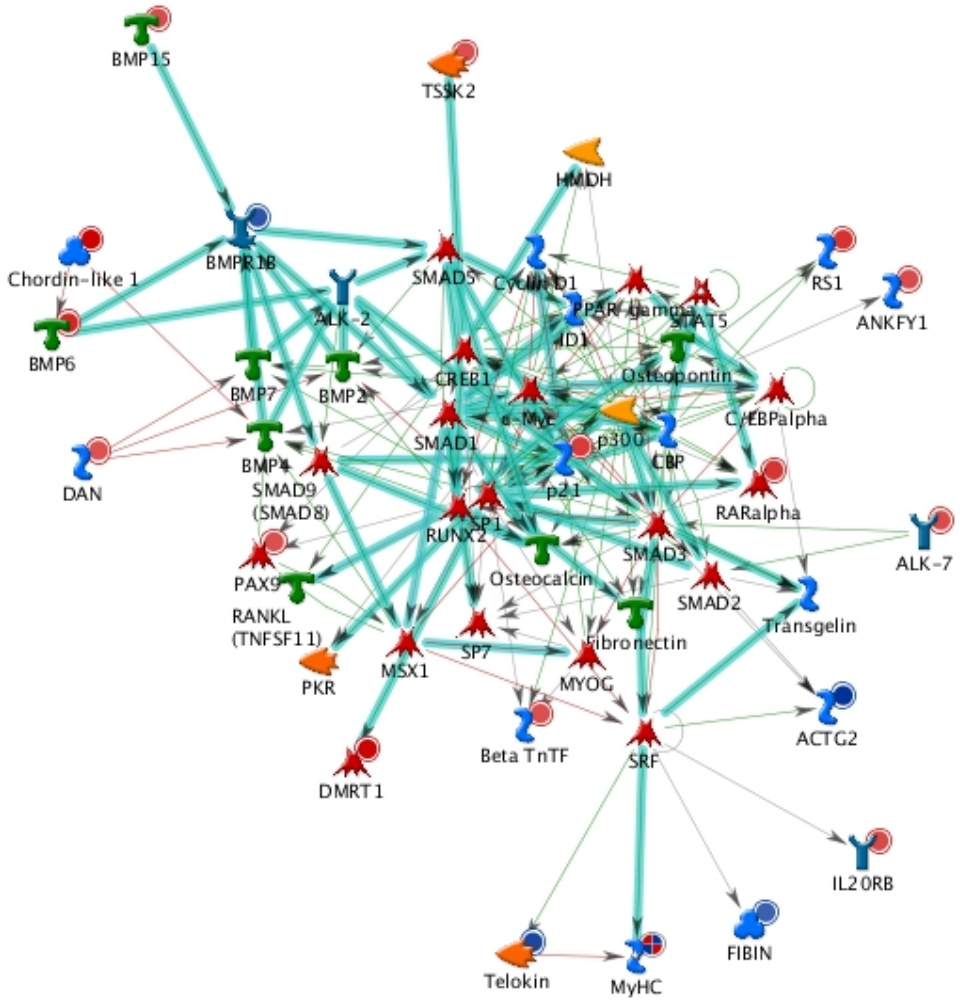


Figure 6.5 Network 1 from AAA unique gene list.

Thick cyan lines indicate the fragments of canonical pathways. Up-regulated genes are marked with red circles; down-regulated with blue circles. The 'checkerboard' colour indicates mixed expression for the gene between files or between multiple tags for the same gene.

Table 6.2 Receptors, transcription factors and protein involved in network 1.

Genes in red are those that are differentially expressed in the experiment.

Transcription factors	Receptors	Protein secreted
c-Myc	**ALK-2**	**BMP** (2 / 4 / 6 / 7)
C/EBPalpha	**IL20RB**	Fibronectin
CREB1	**ALK-7**	Osteocalcin
DMRT1		Osteopontin
MSX1		RANKL
MYOG		
PAX-9		
PPAR-gamma		
RARalpha		
RNX2		
SMAD (1 / 2 / 3 / 5 / 9)		
SP 1/7		
SRF		
Cyclin D1		

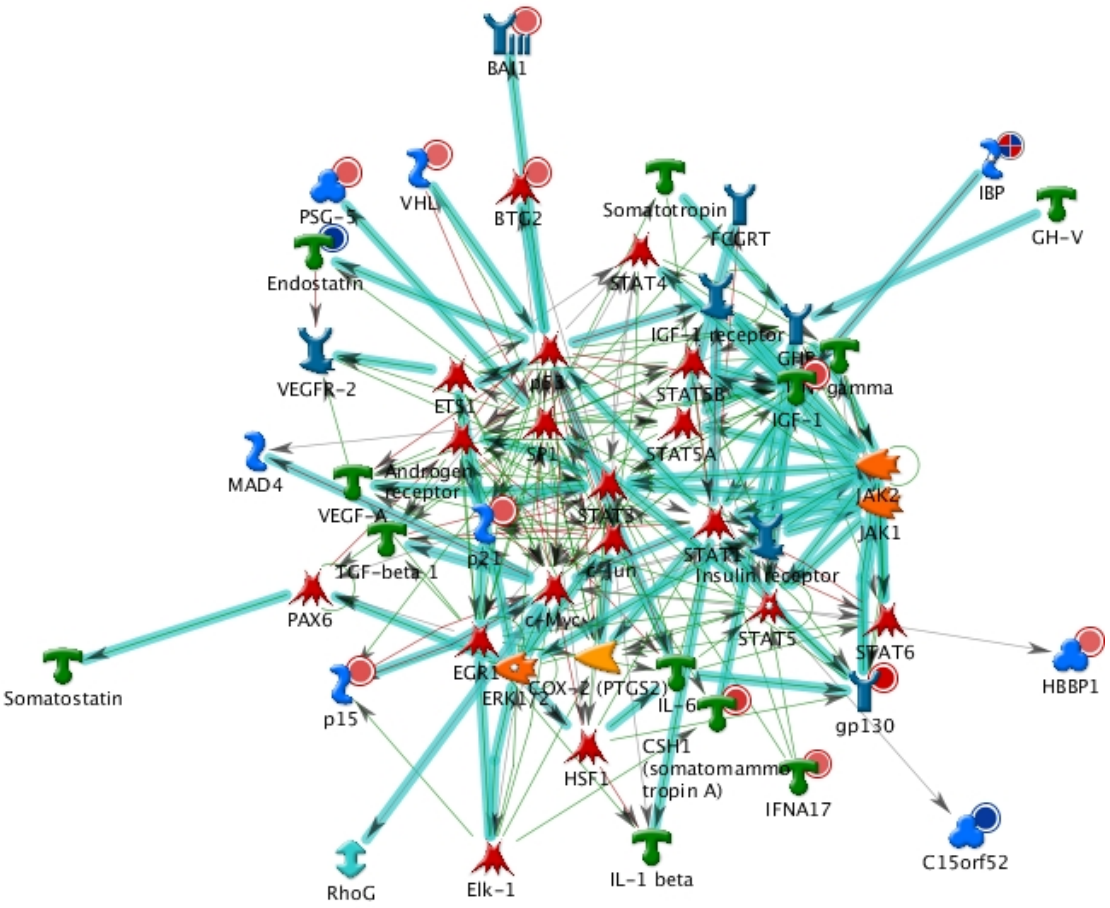


Figure 6.6 Network 2 from AAA unique gene list.

Thick cyan lines indicate the fragments of canonical pathways. Up-regulated genes are marked with red circles; down-regulated genes with blue circles. The 'checkerboard' colour indicates mixed expression for the gene between files or between multiple tags for the same gene.

Table 6.3 Receptors, transcription factors and protein involved in network 2.

Genes in red are those that are differentially expressed in the experiment.

Transcription factors	Receptors	Protein secreted
Androgen receptor	FCGRT	**CSH1**
BTG2	GHR	Endostatin
c-Jun	gp130	IFN- gamma
c-Myc		IGF -1
EGR1		IL -1β
ELK-1		**IL-6**
ETS-1		Somatostatin
HSF-1		Somatotropin
p53		TGF – β1
PAX6		VEGF -A
SP1		
STAT 1/3/4/5/6		

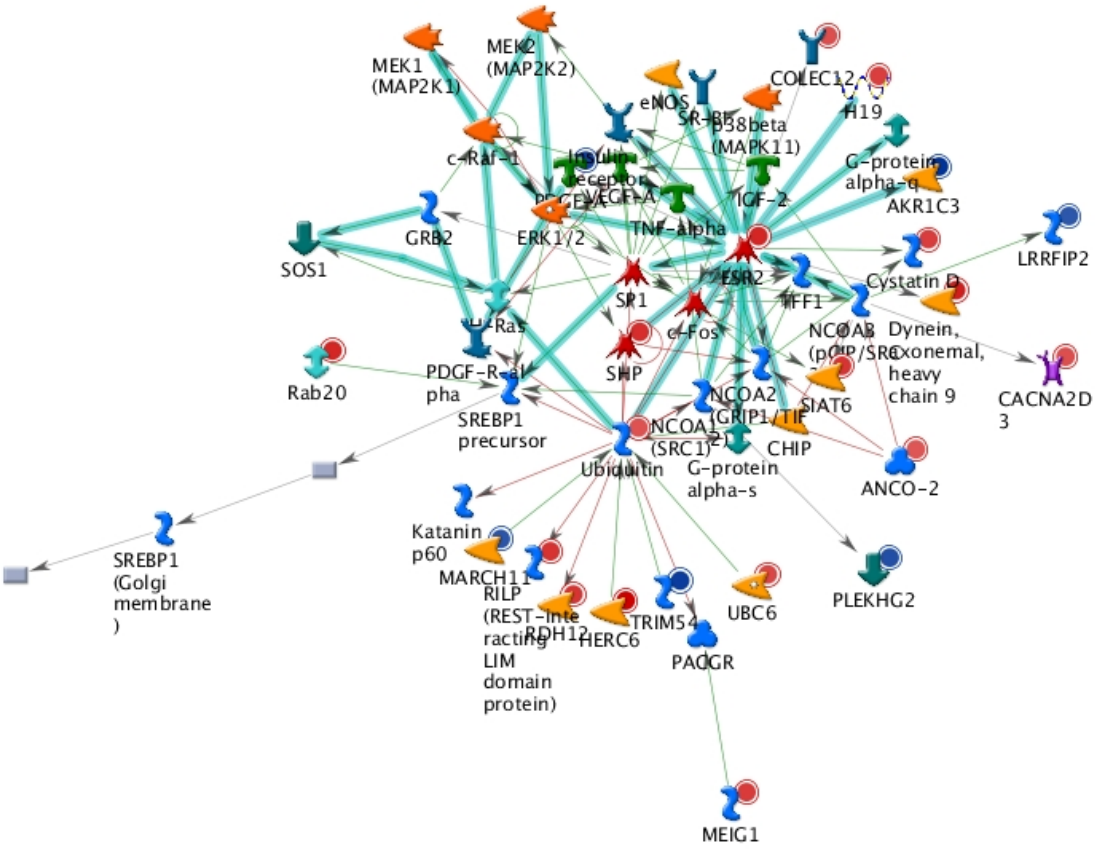


Figure 6.7 Network 3 from AAA unique gene list.

Thick cyan lines indicate the fragments of canonical pathways. Up-regulated genes are marked with red circles; down-regulated genes with blue circles. The 'checkerboard' colour indicates mixed expression for the gene between files or between multiple tags for the same gene.

Table 6.4 Receptors, transcription factors and protein involved in network 3.

Genes in red are those that are differentially expressed in the experiment.

Transcription factors	Receptors	Protein secreted
C –Fos	**COLEC12**	IGF – 2
ESR – 2	SR – B1	**PDGF – A**
SHP		TNF - α
SP1		VEGF - A

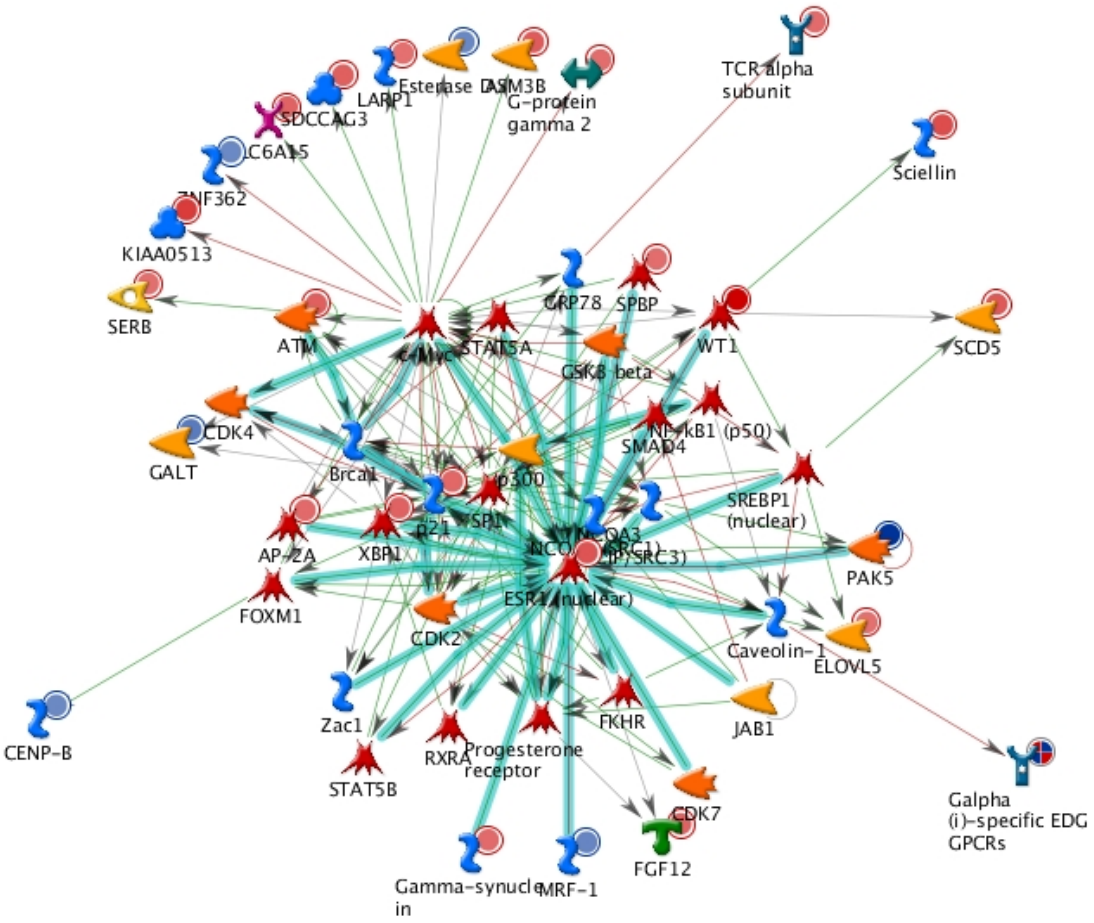


Figure 6.8 Network 4 from AAA unique gene list.

Thick cyan lines indicate the fragments of canonical pathways. Up-regulated genes are marked with red circles; down-regulated genes with blue circles. The 'checkerboard' colour indicates mixed expression for the gene between files or between multiple tags for the same gene.

Table 6.5 Receptors, transcription factors and protein involved in network 4.

Genes in red are those that are differentially expressed in the experiment.

Transcription factors	Receptors	Protein secreted
AP-2A	G alpha (i) specific EDG	**FGF-12**
cMyc	TCR alpha subunit	
ESR1		
FKHR		
FOXM1		
NF – κB		
Progesterone receptor		
RXRA		
SMAD4		
SP1		
SREBP1		
STAT5A		
STAT5B		
WT1		
XBP1		

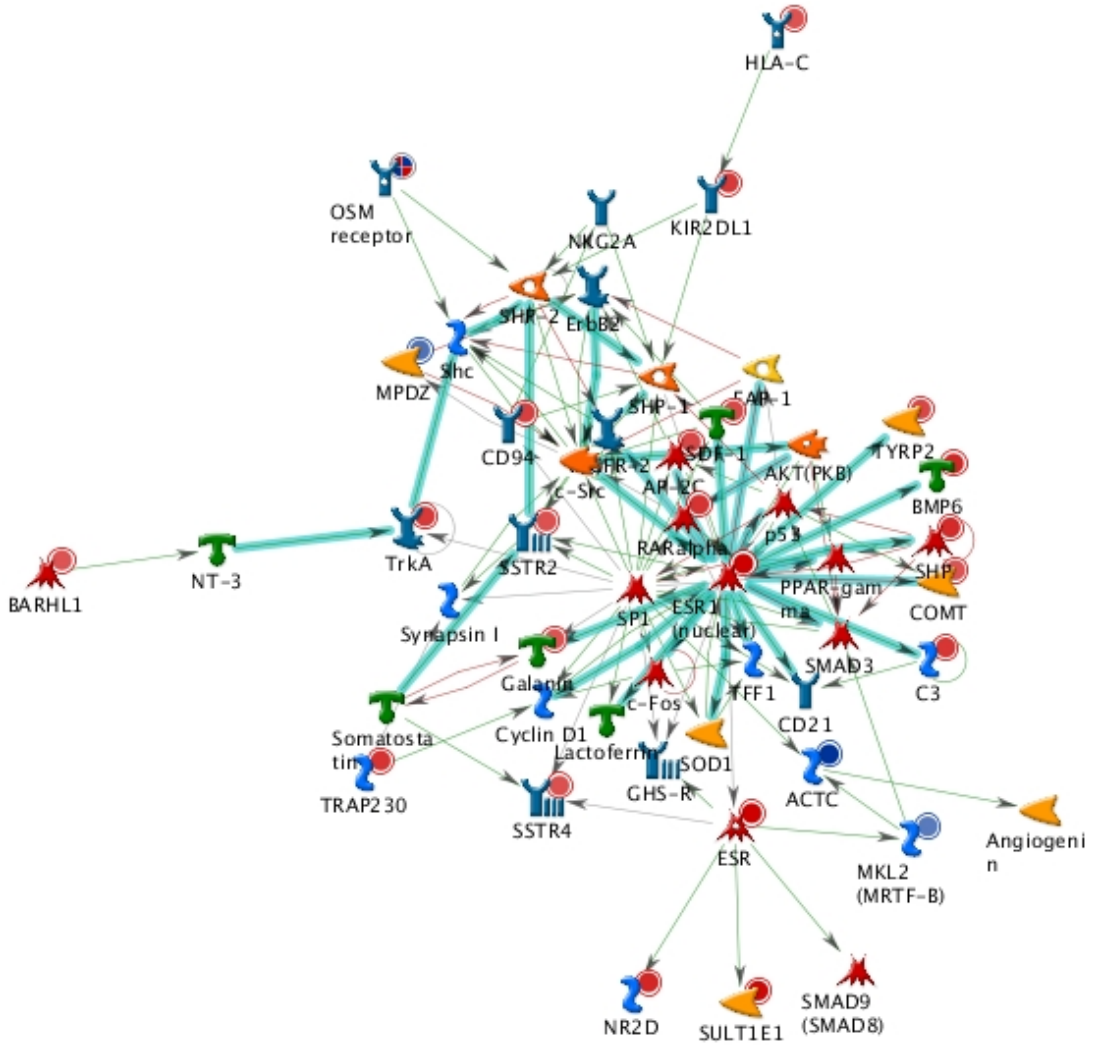


Figure 6.9 Network 5 from AAA unique gene list.

Thick cyan lines indicate the fragments of canonical pathways. Up-regulated genes are marked with red circles; down-regulated with blue circles. The 'checkerboard' colour indicates mixed expression for the gene between files or between multiple tags for the same gene.

Table 6.6 Receptors, transcription factors and protein involved in network 5.

Genes in red are those that are differentially expressed in the experiment.

Transcription factors	Receptors	Protein secreted
AP-2C	CD21	**BMP6**
c-Fos	CD94	**Galanin**
ESR	**KIR2DL1**	Lactoferrin
ESR1	NKG2A	NT – 3
p53		**SDF – 1**
PPAR – gamma		Somatostatin
RAR – alpha		
SHP		
SMAD3		
SMAD9		
SP1		

6.4 Discussion

6.4.1 Pathway analysis

Inflammation is an important feature of the remodelling process involved in human AAA formation[304]. This was reflected by a predominance of inflammatory pathways which were significantly enriched by differentially expressed genes which are unique to AAA. All components of the complement system (alternative, classical and lectin) featured strongly among the top pathway maps. The complement system plays an important role in host innate humoral immunity. The basic functions of complement are opsonisation, chemotaxis for macrophages and neutrophils, lysis of antigens, debris removal and response to tissue injury[305;306]. Complement activation generates the anaphylatoxins C3a and C5a, which are potent leukocyte chemoattractants[307]. Involvement of the complement system in the pathophysiology of AAA has been demonstrated in an elastase-induced mice model of AAA[308]. A deficiency in complement activity (antibody depletion) protected mice against AAA compared with controls. Activation of the complement pathway led to the recruitment of neutrophils to the aortic wall with generation of neutrophil associated proteases (including potent elastases) that are important in AAA development[308]. The presence of complement fixing IgG subclasses along with increased C3 has been demonstrated using immunocytochemistry in human AAA wall[309]. Further studies investigating expression and activity of complement at different stages of AAA expansion are needed to elucidate the direct involvement of complement in human AAA development.

IRE1 is an ER (endoplasmic reticulum) localised transmembrane protein that is upregulated in this study. IRE1 increases the expression of stress response genes through mRNA processing[310] and attenuates the response of several genes by cleavage of mRNA[311]. One of the cleavage targets is CD59 whose expression is reduced in human cultured cells when IRE1 is overexpressed [312]. CD59 is a glycoprotein that regulates human complement–mediated cell lysis by inhibiting assembly of the membrane attack complex (MAC)[313]. CD59 binds complement C8 and / or C9 during assembly of MAC, thereby inhibiting inclusion of multiple copies of C9 into the complex, which is necessary for osmolytic pore formation[313]. Deficiency of CD59 has been shown to accelerate AAA in angiotensin II induced ApoE null mice (complement depleted) model of AAA. It is postulated that deficiency of CD59 results in overexpression of MAC which induces upregulation of MMP-2 and MMP-9[314]. These proteolytic enzymes are thought to play a role in AAA pathogenesis[315]. MAC is also chemotatic for macrophages[314] which are a source of MMP-9[316].

Nuclear factor of activated T-cells (NFATs) are calcium dependent transcription factors, activated by stimulation of receptors coupled to calcium/calcineurin signals, such as the antigen receptors on T-Cells and B-Cells[317]. NFAT signalling plays an important role in cell-cell communication among different cells of the immune system[318]. It is also critical in the expression of a number of immmunologically important genes, including a wide array of cytokines: interleukins (IL-2 , IL-3, IL-4, IL-5 IL-6, IL-10 and IL-13) , interferon-gamma (IFN -γ), tumour necrosis factor-alpha (TNF-α),and granulocyte-macrophage colony-stimulating factor (GMCSF),as well as several related membrane-bound proteins such as CD40 ligand (CD40L), fas ligand

(Fas L) and cytotoxic T- lymphocyte-associated antigen-4 (CTLA4)[318;319]. A putative role for interleukins in AAA has been confirmed in a number of studies. Serum levels of IL-2 and IL-6 have been shown to be higher in AAA patients compared with controls[320]. TNF may be involved in AAA expansion through VSMC apoptosis[321], proteolytic breakdown of the extracellular matrix[321] and induction of inflammatory and immunological processes[322;323]. Serum levels of TNF are elevated in patients with AAA compared with healthy individuals and correlate positively with aneurysm size[320]. IFN-γ inhibits collagen production by VSMC in the aortic wall[324]. Its serum concentrations have also been shown to correlate with AAA expansion[325]. CD40L has been shown to enhance mRNA and protein production of MMP-2 in cultured AAA tissues[326]. Trapidil, a CD40-CD40L pathway inhibitor, has a potential therapeutic role in AAA[326]. The NFAT signalling pathway is thus critical in immune response and an understanding of its biochemistry will allow development of more selective and efficient pharmaceuticals that suppress, modify, or augment immune responses in AAA development.

6.4.2 Network analysis

6.4.2.1 Network 1

The top scoring network (Network 1) identified several transcription factors: doublesex and mab-3 related transcription factor-1 (DMRT1), paired box gene-9 (PAX-9) and retinoic acid receptor - alpha (RAR-α) which were upregulated in AAA. Bone morphogenic protein (BMP) genes feature prominently in this pathway. Upregulation of BMP-6 has been confirmed on qRT-PCR in this experiment (Section

6.3) and its possible role in the pathogenesis of AAA will be discussed in Section 7.1. Other genes of interest are IL20RB and p21. IL20 and its receptors belong to the IL10 family of cytokines and play a role in skin inflammation[327] and development of hematopoietic cells. IL20RB is expressed on human endothelial cells[328] and binding of IL20 to its receptors induces upregulation of VEGF and bFGF[329] and angiogenesis in human umbilical vein endothelial cells. Both of these angiogenic genes have been implicated in the pathogenesis of AAA[145]. IL20 also increases the expression of MMP-2[329] , a proteolytic enzyme involved in degradation of elastin and AAA expansion[330]. p21 is a potent cyclin-dependent kinase inhibitor involved in apoptosis following caspase activation[331]. Upregulation of p21 is a putative mechanism involved in VSMC apoptosis in AAA formation[332].

RAR-α is a drug target (Tamibarolene, Isotretinonin, Retinoic acid) for Network 1. This gene has been implicated in a myriad of functions including apoptosis[333], differentiation[333], granulopoeisis[333] and transcription of clock genes[334]. Retinoids are increasingly being used for remission of cancer[334] and are being tested to limit neointimal proliferation in vascular disease such as atherosclerosis and hypertension[335;336]. Retinoic acid has been shown to induce vascular remodelling in rat aortic smooth muscle cells through modulation of vascular integrins[337]. VSMC depletion is a feature of AAA formation and therefore maintenance of VSMC integrity is important to prevent remodelling of the aortic wall.

6.4.2.2 Network 2

A different set of pathways are involved in Network 2 with expression of a different set of transcription factors. A possible role for IL-6 in AAA formation has been demonstrated in previous studies[338;339]. Janus kinase (Jak) induced tyrosine phosphorylation of the signal transducer and activator of transcription (STAT) is a primary mediator of IL-6 induced signalling [340]. The Jak-STAT pathway controls genes that are important in macrophage activation and vascular remodelling[340]. The IL-6 induced Jak-STAT signalling cascade has been shown to be activated in angiotensinII infused rats which induces AAA formation[341]. B-cell translocation gene 2 (BTG-2) has anti-proliferative properties, but its role in vascular disease has not been elucidated yet[342]. Brain – specific angiogenesis inhibitor -1 (BAI-1), which is expressed downstream of the BTG -2 pathway, is known to regulate angiogenesis[343].

Insulin growth factor -1 (IGF-1) is a possible therapeutic target. IGF-1 has potent collagen and proteoglycan stimulating activity[344] and its concentration is decreased in human aortic aneurysm wall compared with normal aorta at the protein level[345]. IGF-1 has a role in the deregulation of collagen metabolism in AAA[345]. Simvastatin downregulates IGF-1 receptor[346] and can reduce AAA expansion rate[347]. Its other activities such as inhibition of cathepsin and MMPs may also be involved.

6.4.2.3 Networks 3-5

The three remaining networks show an overlap of a number of genes and pathways. The oestrogen receptor (ESR 1, ESR 2 and ESR3) are present in all three remaining networks. Oestrogen receptors are known to have a major role in vascular physiology[348]. In primates fed with atherogenic diets oestrogen supplementation inhibited collagen accumulation and elastin loss in the abdominal aorta[349]. These changes could predispose to AAA development. ESR-2 polymorphism has also been put forward as a genetic determinant in AAA in human[350].

Pathway analysis has revealed novel genes upstream or downstream of a specific gene known to be involved in AAA formation. Novel pathways that may be involved in AAA pathogenesis have also been identified.

Chapter 7

Discussion, future work and conclusions

7.1 General Discussion

This is the first whole transcriptome analysis investigating tripartite differential gene expression in the wall of AAA, AOD and normal abdominal aorta. This study has unravelled novel genes and pathways with potential roles in the pathogenesis of AAA. By comparing AAA with AOD, the gene set has been reduced considerably probably shifting the emphasis on genes that are more relevant in AAA formation. The results from these experiments are robust as they have passed all the stringent criteria for quality control of microarray analysis. A small number of these differentially expressed genes were confirmed by qRT-PCR. The large numbers of genes that are differentially expressed support the notion that AAA is a polygenic disorder.

7.1.1 Comparison with other microarray studies

There have been two studies of gene expression profiling in AAA and NA using limited arrays. Absi et al[95] used an array of 1185 genes and showed differential expression of 104 genes (65 increased and 39 decreased). A large number of these differentially expressed genes were confirmed in our whole genome microarray analysis. Tung et al[135] used an array of 1176 genes. Four out of the six most upregulated genes (MMP-9, Cathepsin H, myeloid cell nuclear differentiation antigen and platelet derived growth factor A) and both of the most downregulated genes (myosin light chain kinase and integrin β1) were also found to be differentially expressed in this study.

Armstrong et al[250] evaluated differential gene expression in AAA, AOD and NA using a 225 genes array. They found that there was no differential expression of the matrix metalloproteinase or tissue inhibitors of metalloproteinase. This is in accordance with the results of this study with the exception that we have shown MMP-3 to be differentially expressed, confirming our previous work[123]. Increased expression of laminin α4 and insulin receptor in AOD and decreased expression in COL6A1, Glycoprotein IIIA and α2 – macroglobulin in AAA were also reflected in our study. The high confirmatory rate and reproducibility between the current study and the previous micro-array studies provides support for the robustness of our data.

7.1.2 Genes differentially expressed on chromosomes 4q31 and 19q13

Chromosomes 4q31 and 19q13 have been identified as susceptible loci for AAA[240]. We found no differentially expressed genes between AAA and AOD located on chromosome 4q31, while three genes (Spi-B transcription factor, CD79A and RYR1) were differentially expressed on 19q13. Two of these, Spi-B transcription factor and CD79A, were subsequently confirmed on both microarray and qRT-PCR although RYR1 was not assessed by qRT-PCR.

CD79A is a B-lymphocyte antigen receptor[351]. It is expressed during both the early stage of B lymphoblast and terminal stage of plasma cells. CD79a thus plays a key role in B-cell development, stabilisation and function[352;353].

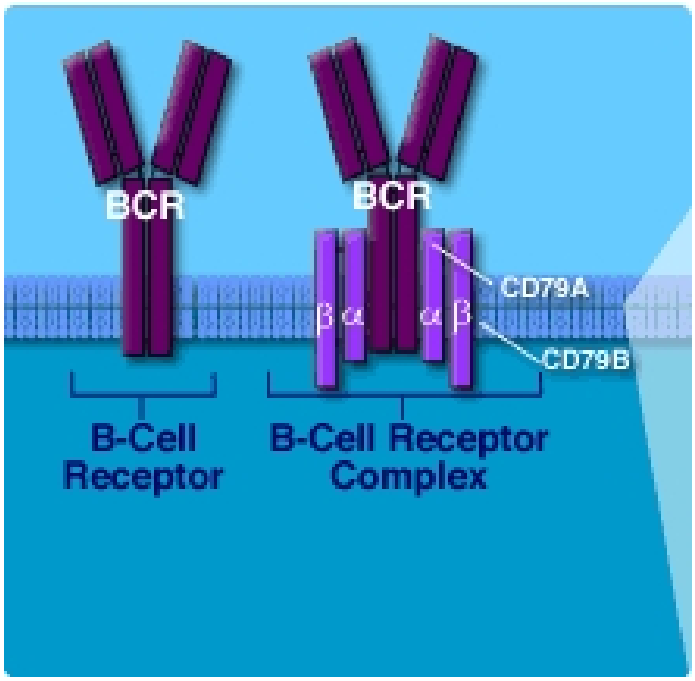


Figure 7.1 BCR – B cell receptor.

CD79A is associated with the BCR complex. When the BCR complex is activated by binding of antigen it causes growth and proliferation of B-cells[354]. An increased concentration of B-cell infiltrates has been shown in the adventitia of AAA wall[109]. B cell is also an important source of immunoglobulins and this study has also demonstrated a higher expression of genes expressing autoantibodies in the walls of AAA. IGHA1 , also known as IGA, showed the highest differential expression in AAA compared with AOD or NA and its presence has been previously demonstrated with a trend towards a higher proportion of IgA with increasing thickness of the wall[355].

Spi-B is a member of a family of ETS transcription factors[356]. Spi-B is expressed in plasmacytoid dendritic cell precursors and it modulates the development of T-cells, B-cells and Natural Killer cells[357;358]. These cells are important inflammatory mediators in AAA formation[98;101]. Their presence in AAA wall has been confirmed in previous studies[97;98;101] and they are responsible for the Th1/Th2 response that leads to AAA formation in mouse models[105].

RYR1 (Ryanodine receptor 1) is also located on chromosome 19q13. It increases the expression of major histocompatibility complex II molecules on the surface of dendritic cells and thus may play a role in inflammatory responses in AAA[359].

7.1.3 Inflammation

The large number of inflammatory genes that were up-regulated in AAA vs. AOD and AAA vs. NA in this study highlights the importance of inflammation in AAA. Among the genes with the highest fold-change (i.e. first 20 genes in either AAA vs. AOD or AAA vs. NA), there was a predominance of inflammatory genes (55% in AAA vs. AOD and 75% in AAA vs. NA). This is in agreement with a previous whole transcriptome analysis comparing AAA with NA[96]. When comparing AAA with AOD, there was an increased incidence of genes that were related to B-cells. CD19, a B-cell marker[360], was upregulated in AAA wall on both micro array and RT-PCR analysis in our study. There is ,however, evidence to suggest that AAA is a specific antigen driven T-cell disease[99-101].These studies have also confirmed the presence of B cells in AAA wall[99;100] and one of the studies[101] looked specifically at

immunophenotypes of the intraluminal thrombus in AAA rather than AAA wall. Cells present in the thrombus vary from those present in the aortic wall[361]. T-cells also play an important role in atherosclerosis[362;363]. This could explain the lower incidence of T-cells related genes in comparing AAA with AOD. When comparing AAA vs. NA, markers of T-cells e.g. CD69 and CD3 were highly differentially expressed (fold-change of 12 and 9, respectively). $CD3^+$ T cells account for approximately 50% of hemopoetic cells that have been recovered from aortic tissues[99-101]. $CD69^+$ T cells are expressed at an early stage of AAA development[108].

Other inflammatory genes of interest that we found differentially expressed were toll-like receptor (TLR10) which has a fundamental role in pathogen recognition and activation of innate immunity[364]. TLRs recognise pathogens at the cell surface[365]. Several microbial pathogens[113] that have been proposed as culprits in AAA formation including Salmonella, Chlamydia, CMV and treponoma are capable of interacting with TLRs. The interaction between the TLR and the microbial component triggers the activation of signalling cascades leading to induction of genes producing pro-inflammatory cytokines and type I interferons[366]. Increased expression of TLR4 RNA and protein was found in cerebal aneurysm in humans[367].

The chemokines CCL13 and CX3CR1 were upregulated in AAA compared with AOD or NA. CCL13 plays a role in the accumulation of leukocytes during inflammation. It may be involved in the recruitment of monocytes in the arterial wall[368]. CX3CR1, fractalkine receptor, expressed on natural killer cells and T cells, has been shown to

be present in AAA wall and through its interaction with CX3CL1 may contribute to recruitment of inflammatory cells in AAA tissues[369].

IL7[370] and IL2RG[371], which were overexpressed in AAA in our study, are interleukins whose role in AAA are yet to be determined but are known to be important mediators of inflammation.IL-7[372] and IL2RG[373] are both important for B and T- cell development.

7.1.4 Proteolysis

MMPs .The matrix metallopeptidases have been extensively studied in the proteolytic breakdown of AAA wall[122;193;374]. Only MMP-3 was upregulated in AAA when compared with either AOD or NA. MMP9 was highly expressed in both AAA and AOD compared with NA. These results are in agreement with those of two other studies of MMP expression at the transcriptional level[123;250] suggesting that MMP-9 is more a marker of atherosclerosis. The presence of the 5A allele in the promoter region of the MMP-3 gene is associated with increased MMP-3 production and increased risk of developing AAA[191-194]. MMP-3 activity might therefore be a useful target for the treatment of AAA.

Cathepsins. These proteolytic enzymes have potent collagenase and elastase activities[131]. Cathepsins D, H and L degrade structural proteins and there is greater activity of these enzymes in AAA wall and mural thrombus than in normal aortic wall[132;135;140;375]. Cathepsin H was the only cysteine protease that was upregulated

when comparing AAA with AOD[67] although cathepsins D and K mRNA were higher in AAA vs. NA in this study. Cathepsin L expression is downregulated in AAA and is associated with atherosclerosis[376].

ADAMTS. ADAMTS-6 and ADAMTS-9 form part of a family of metalloproteases that play an important role in the turnover of extracellular matrix proteins in various tissues and have been implicated in atherosclerosis[377]. Both genes were downregulated in this study although downregulation of ADAMTS-9 was not confirmed by qRT-PCR for putative reasons elaborated on in the previous chapter.

Surprisingly, few genes regulating proteolysis were upregulated with twice as many downregulated when comparing AAA with AOD suggesting that remodelling of the aortic wall in AAA and AOD might involve to some extent a common set of genes.

7.1.5 Apoptosis

VSMCs apoptosis plays an important role in AAA development[147;148;378]. This study confirmed upregulation of genes that have been previously studied in AAA: caspases, Fas, p53 and TIMP-3[123;378;379]. Activin A receptor type IC (ACVR1C) showed the highest fold change in either group. It induces apoptosis through activation of TGFβ pathways[150] which have been implicated in AAA formation[150]. SPEG has a role in the regulation and differentiation of VSMCs and is associated with atherosclerosis[380].

7.1.6 Angiogenesis

The medial layer of the infra-renal abdominal aorta is devoid of vasa vasorum[141]. Neovascularisation of the medial layer is however an established feature of AAA[142]. These microvessels allow entry of inflammatory cells into the media leading to extracellular matrix degradation[144]. Angiogenesis is thus important for AAA development. In the angiogenic group, two HOX genes were upregulated when comparing AAA with AOD. Both genes maintain endothelial cells in a non-angiogenic differentiated stage[381;382]. VEGF and IL-8 were highly expressed in both AAA and AOD.

7.1.7 Bone morphogenic protein 6

Bone morphogenic protein 6 (BMP-6) was one of the upregulated microarray genes that was confirmed by RT-PCR. BMP-6 belongs to the TGF-β superfamily and has a variety of roles in different cell types. BMP-6 has a role in immune response pathways and inhibits cell growth in mature B cells[383], which we know are present in large numbers in AAA wall. Endogenous BMP-6 increases aldosterone production through angiotensin II related pathways[384]. This may be crucial in AAA development as increased aldosterone and angiotensin II are associated with hypertension that is a major risk factor for AAA.

BMP-6 increases the level of osteopontin (OPN)[384], a gene implicated in the pathogenesis of AAA formation[384].OPN is a phosphorylated acidic glycoprotein that has been implicated in vascular calcification. OPN is not found in normal arteries but

is abundant at sites of calcification in human atherosclerotic plaques[385]. In mouse models, OPN inhibits arterial calcification which is inversely correlated to the growth rate of small AAAs[385;386]. Thus, increased level of OPN in aortic wall will predispose to AAA formation. The ability of BMP-6 to influence the above pathways makes it an interesting therapeutic target to limit AAA formation.

7.2 Limitations of this study

A major limitation of this study is that differential expression of genes in AAA was investigated in the patients who were undergoing elective repair and therefore the AAAs were always larger than 5 cm. The gene profile would therefore represent expression during 'late stage 'disease, which may be considerably different from the transcriptional profile at an earlier stage of AAA development. Obtaining tissues from patients with small aneurysms is ethically not possible and animal models of AAA development may not be totally representative of the processes that lead to AAA development in man. Differentially expressed genes also need to be confirmed at the protein level, as it is well recognised that RNA expression does not always lead to protein production[387] and many post translational processes such as glycosylation and phosphorylation affect final protein activity and function.

Normal aortic tissues were obtained from organ donors who are relatively younger than patients with AAA and AOD and therefore it was difficult to match these accurately for demographic and vascular risk factors. Comparison between AAA and AOD removes age and atherosclerosis as confounding variables. There are

however, morphological differences in the aortic walls of AAA and AOD. AAA is mainly a disease of the media while AOD is a diseae of the intima suggesting that different molecular processes may be involved in the formation of the atherosclerotic plaques.

The samples of AAA used were of high quality as they were harvested fresh from theatre. AOD and normal aorta samples were archived specimens which showed increased amount of degraded RNA. This selection bias may, to some extent, skew the results obtained.

Despite, these limitations, this study provides an insight into the differential gene expression patterns in large AAA compared with stenosing disease of the aorta which has atherosclerosis as a common denominator, but results in different pathology.

7.3 Future work and conclusions

The differential expression of a number of novel genes has been elucidated and the next steps would be to confirm the expression of these genes at the translational and activity level.

Factors that are confirmed to be differentially expressed at the protein and activity level should also be investigated at different stages during AAA development in mouse models of disease such as the ApoE mouse Angiotensin II infusion model[388].

Low concentrations of Angiotensin II infused gives rise to a slow AAA formation[389] and this would allow sampling windows at early, mid and late stage development of AAA. The importance of a factor that is shown to correlate strongly with AAA development could then be studied by cross-breeding ApoE mice with mice that have a total deficiency (knockout) or are conditional knockout or knockin (e.g. no or overexpression in macrophages) for a particular factor. AngII–induced AAA development could then be assessed in these transgenic mice.

Comparison of genetic and expression data could lead to the elucidation of novel pathways that could be targeted for the medical management of AAA.

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Appendices

Appendix A: Reagents and materials used

Appendix B: Genes upregulated in AAA vs. AOD

Appendix C: Genes downregulated in AAA vs. AOD

Appendix D: Genes upregulated in AAA vs. NA

Appendix E: Genes downregulated in AAA vs. NA

Appendix F: Inflammatory genes AAA vs. AOD

Appendix G: Proteolytic genes in AAA vs. AOD

Appendix H: Apoptotic genes in AAA vs. AOD

Appendix I: Angiogenic genes in AAA vs. AOD

Appendix J: Inflammatory genes in AAA vs. NA

Appendix K: Proteolytic genes in AAA vs. NA

Appendix L: Apoptotic genes in AAAA vs. NA

Appendix M: Angiogenic genes in AAA vs. NA

Appendix N: Legends to pathways and networks

Appendix O: PCR raw data

APPENDIX A: Reagents and materials used.

Total RNA isolation

Dulbecco's phosphate buffered saline (D-PBS) pH 7.4

TRIzol reagent, Invitrogen Life Technologies

Chloroform 99.5% (Molecular biology grade, Sigma)

Isopropanol 99% (Molecular biology grade, Sigma)

Ethanol 99% (Molecular biology grade, Sigma)

RNAse free- water (Qiagen)

RNeasy Midi Kit, Qiagen

Buffer RW1 (washing buffer)

DNAse I mix

RPE buffer

APPENDIX A: Reagents and materials used (continued).

Micro-array target labelling

One-cycle cDNA synthesis kit (Affymetrix)

T7-Oligo (dT) Primer, 50μM

5 × 1st Strand reaction mix

DTT, 0.1M

dNTP, 10mM

SuperScript II, 200U/μL

5× 2nd strand reaction mix

E Coli DNA ligase, 10U/μL

E Coli DNA polymerase , 10U/μL

RNAseH, 2U/μL

T4 DNA Polymerase , 5U/μL

EDTA, 0.5M

RNAse free-water

Sample cleanup module kit (Affymetrix)

cDNA binding buffer

cDNA cleanup spin column

cDNA wash buffer

cDNA elution buffer

APPENDIX A: Reagents and materials used (continued).

5×- Fragmentation buffer

2-mL collection tube

IVT labelling kit (Affymetrix)

10× - IVT labelling buffer

IVT labelling NTP mix

IVT labelling enzyme mix

Sample clean-up module (Affymetrix)

IVT binding buffer

IVT cRNA clean-up spin column

IVT cRNA wash buffer

Genechip hybridization, wash and stain kit (Affymetrix)

Control oligonucleotide B2 (3nM)

20 × eukaryotic hybridization controls

Herring sperm DNA (10mg/ml)

BSA (50mg/ml)

2 × hybridization buffer

DMSO

APPENDIX A: Reagents and materials used (continued)

qRT-PCR reaction

RT step (Enhanced avian RT first strand synthesis kit, SIGMA)

Deoxynucleotide mix (10mM dATP, 10mM dCTP, 10mM dTTP, 10mM dGTP)

Random nanomers

Enhanced Avian Reverse Transcriptase (solution in 200mM KH_2PO_4, pH 7.2, 2mM DTT, 0.2% Triton, 50% glycerol)

10 × buffer for eAMV Reverse Transcriptase , 500mM Tris-HCL, pH 8.3, 400mM KCL, 80mM $MgCl_2$, 10mM DTT)

PCR step (TaqMan gene expression assays, Applied Biosystems)

TaqMan gene expression assays (20×)

TaqMan Universal PCR Master Mix (2×)

TaqMan Fast Universal PCR Master Mix (2×)

Appendix B: Genes upregulated in AAA vs. AOD

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
230673_at	polycystic kidney and hepatic disease 1 (autosomal recessive)-like 1	PKHD1L1	93035	32
217378_x_at	similar to Ig kappa chain precursor V region (orphon V108) - human (fragment)	LOC391427	391427	23
203000_at	stathmin-like 2	STMN2	11075	22
214916_x_at	immunoglobulin heavy locus		283650	18
217480_x_at	similar to Ig kappa chain	LOC339562	339562	15
215946_x_at	similar to omega protein	LOC91353	91353	14
234884_x_at	Immunoglobulin lambda joining 3	IGLC2	3538	14
228335_at	claudin 11 (oligodendrocyte transmembrane protein)	CLDN11	5010	12
225792_at	Hook homolog 1 (Drosophila)	HOOK1	51361	12
216207_x_at	immunoglobulin kappa variable 1D-13	IGKV1D-13	28902	11
220059_at	BCR downstream signaling 1	BRDG1	26228	10
210121_at	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2	B3GALT2	8707	9
212592_at	Immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	IGJ	3512	8
210356_x_at	membrane-spanning 4-domains, subfamily A, member 1	MS4A1	931	7
207031_at	bagpipe homeobox homolog 1 (Drosophila)	BAPX1	579	6
1555779_a_at	CD79A antigen (immunoglobulin-associated alpha)	CD79A	973	6
220068_at	pre-B lymphocyte gene 3	VPREB3	29802	6
235982_at	Fc receptor-like 1	FCRL1	115350	6
235965_at	DKFZP434B0335 protein	DKFZP434B0335	25851	6
221239_s_at	Fc receptor-like 2 ; Fc receptor-like 2	FCRL2	79368	6
221969_at	Paired box gene 5 (B-cell lineage specific activator)	PAX5	5079	5
219667_s_at	B-cell scaffold protein with ankyrin repeats 1	BANK1	55024	5
228599_at	membrane-spanning 4-domains, subfamily A, member 1	MS4A1	931	5
205671_s_at	major histocompatibility complex, class II, DO beta	HLA-DOB	3112	5
227224_at	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	55103	5

Appendix B: Genes upregulated in AAA vs. AOD (continued)

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
229400_at	homeo box D10	HOXD10	3236	4
219197_s_at	signal peptide, CUB domain, EGF-like 2	SCUBE2	57758	4
232739_at	Spi-B transcription factor (Spi-1/PU.1 related)	SPIB	6689	4
226435_at	papilin, proteoglycan-like sulfated glycoprotein	PAPLN	89932	4
239349_at	C1q and tumor necrosis factor related protein 7	C1QTNF7	114905	4
227533_at	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	55103	4
217767_at	complement component 3	C3	718	4
206398_s_at	CD19 antigen	CD19	930	4
205692_s_at	CD38 antigen (p45)	CD38	952	4
1563674_at	Fc receptor-like 2	FCRL2	79368	4
213317_at	Chloride intracellular channel 5	CLIC5	53405	4
1558881_at	hypothetical protein LOC145820	LOC145820	145820	4
205898_at	chemokine (C-X3-C motif) receptor 1	CX3CR1	1524	4
1552519_at	activin A receptor, type IC	ACVR1C	130399	4
223751_x_at	toll-like receptor 10	TLR10	81793	4
228377_at	kelch-like 14 (Drosophila)	KLHL14	57565	4
206999_at	interleukin 12 receptor, beta 2	IL12RB2	3595	3
204424_s_at	LIM domain only 3 (rhombotin-like 2)	LMO3	55885	3
213247_at	sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1	SVEP1	79987	3
224009_x_at	dehydrogenase/reductase (SDR family) member 9	DHRS9	10170	3
1553856_s_at	purinergic receptor P2Y, G-protein coupled, 10	P2RY10	27334	3
225706_at	glucocorticoid induced transcript 1	GLCCI1	113263	3
209220_at	glypican 3	GPC3	2719	3
223952_x_at	dehydrogenase/reductase (SDR family) member 9	DHRS9	10170	3
50965_at	RAB26, member RAS oncogene family	RAB26	25837	3

Appendix B: Genes upregulated in AAA vs. AOD (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
236293_at	Ras homolog gene family, member H	RHOH	399	3
225571_at	leukemia inhibitory factor receptor	LIFR	3977	3
219552_at	Sushi, von Willebrand factor type A, EGF and pentraxin domain containing 1	C9orf13	79987	3
220169_at	hypothetical protein FLJ23235	FLJ23235	80008	3
212311_at	KIAA0746 protein	KIAA0746	23231	3
224406_s_at	Fc receptor-like 5 ; Fc receptor-like 5	FCRL5	83416	3
242458_at	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	55103	3
235278_at	chromosome 20 open reading frame 133	C20orf133	140733	3
242517_at	G protein-coupled receptor 54	GPR54	84634	3
221586_s_at	E2F transcription factor 5, p130-binding	E2F5	1875	3
213094_at	G protein-coupled receptor 126	GPR126	57211	3
235372_at	Fc receptor-like and mucin-like 1	FCRLM1	84824	3
222915_s_at	B-cell scaffold protein with ankyrin repeats 1	BANK1	55024	3
200670_at	X-box binding protein 1	XBP1	7494	3
214971_s_at	ST6 beta-galactosamide alpha-2,6-sialyltranferase 1	ST6GAL1	6480	3
210448_s_at	purinergic receptor P2X, ligand-gated ion channel, 5	P2RX5	5026	3
228434_at	butyrophilin-like 9	BTNL9	153579	3
209840_s_at	leucine rich repeat neuronal 3	LRRN3	54674	3
222245_s_at	fer-1-like 4 (C. elegans)	FER1L4	80307	3
219799_s_at	dehydrogenase/reductase (SDR family) member 9	DHRS9	10170	3
227525_at	glucocorticoid induced transcript 1	GLCCI1	113263	3
206030_at	aspartoacylase (Canavan disease)	ASPA	443	3
205083_at	aldehyde oxidase 1	AOX1	316	3
238439_at	ankyrin repeat domain 22	ANKRD22	118932	3
209506_s_at	nuclear receptor subfamily 2, group F, member 1	NR2F1	7025	3

Appendix B: Genes upregulated in AAA vs. AOD (continued)

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
219429_at	fatty acid 2-hydroxylase	FA2H	79152	3
225575_at	leukemia inhibitory factor receptor	LIFR	3977	3
230075_at	RAB39B, member RAS oncogene family	RAB39B	116442	3
223299_at	SEC11-like 3 (S. cerevisiae)	SEC11L3	90701	3
206513_at	absent in melanoma 2	AIM2	9447	3
225700_at	glucocorticoid induced transcript 1	GLCCI1	113263	3
244033_at	chromosome 14 open reading frame 145	C14orf145	145508	3
204777_s_at	mal, T-cell differentiation protein	MAL	4118	3
1554208_at	similar to mouse meiosis defective 1 gene	MGC40042	150365	3
206126_at	Burkitt lymphoma receptor 1, GTP binding protein (chemokine (C-X-C motif) receptor 5)	BLR1	643	3
217369_at	immunoglobulin heavy constant gamma 1 (G1m marker)	IGHG1	3500	3
214203_s_at	proline dehydrogenase (oxidase) 1	PRODH	5625	3
233500_x_at	C-type lectin domain family 2, member D	CLEC2D	29121	3
225912_at	tumor protein p53 inducible nuclear protein 1	TP53INP1	94241	3
203961_at	nebulette	NEBL	10529	3
227198_at	AF4/FMR2 family, member 3	AFF3	3899	3
205297_s_at	CD79B antigen (immunoglobulin-associated beta)	CD79B	974	3
230006_s_at	hypothetical protein DKFZp313A2432	DKFZp313A2432	258010	3
242388_x_at	T-cell activation GTPase activating protein	TAGAP	117289	3
202062_s_at	sel-1 suppressor of lin-12-like (C. elegans)	SEL1L	6400	3
211077_s_at	tousled-like kinase 1 ; tousled-like kinase 1	TLK1	9874	2
237484_at	hypothetical gene supported by AK092637	LOC440087	440087	2
221601_s_at	Fas apoptotic inhibitory molecule 3 ; Fas apoptotic inhibitory molecule 3	FAIM3	9214	2
215343_at	KIAA1509	KIAA1509	440193	2
228368_at	Rho GTPase activating protein 20	ARHGAP20	57569	2

Appendix B: Genes upregulated in AAA vs. AOD (continued)

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
204951_at	ras homolog gene family, member H	RHOH	399	2
206176_at	bone morphogenetic protein 6	BMP6	654	2
220432_s_at	cytochrome P450, family 39, subfamily A, polypeptide 1	CYP39A1	51302	2
219551_at	ELL associated factor 2	EAF2	55840	2
215407_s_at	astrotactin 2	ASTN2	23245	2
205485_at	ryanodine receptor 1 (skeletal)	RYR1	6261	2
205828_at	Matrix metallopeptidase 3	MMP3	4314	2
227834_at	taxilin beta	TXLNB	167838	2
215243_s_at	gap junction protein, beta 3, 31kDa (connexin 31)	GJB3	2707	2
242541_at	ATP-binding cassette, sub-family A (ABC1), member 9	ABCA9	10350	2
202747_s_at	integral membrane protein 2A	ITM2A	9452	2
202295_s_at	Cathepsin H	CTSH	1512	2
223569_at	phosphatidic acid phosphatase type 2 domain containing 1B	PPAPDC1B	84513	2
206407_s_at	chemokine (C-C motif) ligand 13	CCL13	6357	2
1561820_at	sodium channel, voltage gated, type VIII, alpha	SCN8A	6334	2
213844_at	homeo box A5	HOXA5	3202	2
226560_at	Sphingosine-1-phosphate phosphotase 2	SGPP2	130367	2
201004_at	signal sequence receptor, delta (translocon-associated protein delta)	SSR4	6748	2
206896_s_at	guanine nucleotide binding protein (G protein), gamma 7	GNG7	2788	2
230983_at	B-cell novel protein 1	BCNP1	199786	2
230285_at	hypothetical protein DKFZp313A2432	DKFZp313A2432	258010	2
213540_at	hydroxysteroid (17-beta) dehydrogenase 8	HSD17B8	7923	2
236313_at	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)	CDKN2B	1030	2
202746_at	integral membrane protein 2A	ITM2A	9452	2
1554462_a_at	DnaJ (Hsp40) homolog, subfamily B, member 9	DNAJB9	4189	2

Appendix B: Genes upregulated in AAA vs. AOD (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
226145_s_at	Fraser syndrome 1	FRAS1	80144	2
204116_at	interleukin 2 receptor, gamma (severe combined immunodeficiency)	IL2RG	3561	2
223036_at	phenylalanine-tRNA synthetase-like, beta subunit	FARSLB	10056	2
201998_at	ST6 beta-galactosamide alpha-2,6-sialyltranferase 1	ST6GAL1	6480	2
203528_at	sema domain, immunoglobulin domain (Ig)	SEMA4D	10507	2
220338_at	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	55103	2
223435_s_at	protocadherin alpha 9 ;	PCDHA9	56134	2
220941_s_at	chromosome 21 open reading frame 91	C21orf91	54149	2
205752_s_at	glutathione S-transferase M5	GSTM5	2949	2
209292_at	Inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	ID4	3400	2
1561390_at	family with sequence similarity 41, member A, Y-linked	FAM41AY	340618	2
206693_at	interleukin 7	IL7	3574	2
232635_at	chromosome 14 open reading frame 145	C14orf145	145508	2
204949_at	intercellular adhesion molecule 3	ICAM3	3385	2
203608_at	aldehyde dehydrogenase 5 family, member A1 (succinate-semialdehyde dehydrogenase)	ALDH5A1	7915	2
203962_s_at	nebulette	NEBL	10529	2
213954_at	KIAA0888 protein	KIAA0888	26049	2
242104_at	Ankyrin repeat and KH domain containing 1	ANKHD1	54882	2
232011_s_at	microtubule-associated protein 1 light chain 3 alpha	MAP1LC3A	84557	2

APPENDIX C: Genes downregulated in AAA vs. AOD.

Probe	Gene Description	Gene Symbol	Entrez Gene ID	Fold Change
241942_at	peroxidasin homolog-like (Drosophila)	PXDNL	137902	10
235417_at	SPOC domain containing 1	SPOCD1	90853	10
221009_s_at	aortic preferentially expressed gene 1	APEG1	10290	8
203665_at	angiopoietin-like 4	ANGPTL4	51129	7
222939_s_at	heme oxygenase (decycling) 1	HMOX1	3162	7
235548_at	solute carrier family 16 (monocarboxylic acid transporters), member 10	SLC16A10	117247	5
218975_at	hypothetical protein FLJ90166	FLJ90166	164284	5
223333_s_at	collagen, type V, alpha 3	COL5A3	50509	5
1553449_at	hypothetical protein FLJ36701	FLJ36701	283860	4
210170_at	PDZ and LIM domain 3	PDLIM3	27295	4
1555826_at	Effector cell peptidase receptor 1	BIRC5	332	4
201389_at	integrin, alpha 5 (fibronectin receptor, alpha polypeptide)	ITGA5	3678	4
230333_at	Spermidine/spermine N1-acetyltransferase	SAT	6303	4
205860_x_at	folate hydrolase (prostate-specific membrane antigen) 1	FOLH1	2346	4
209081_s_at	collagen, type XVIII, alpha 1	COL18A1	80781	4
219148_at	PDZ binding kinase	PBK	55872	3
243555_at	Endothelin receptor type A	EDNRA	1909	3
228176_at	endothelial differentiation, sphingolipid G-protein-coupled receptor, 3	EDG3	1903	3
241473_at	Sulfatase 1	SULF1	23213	3
1558199_at	fibronectin 1	FN1	2335	3
52255_s_at	collagen, type V, alpha 3	COL5A3	50509	3
1566785_x_at	Ribosomal protein S7	NSF	4905	3
229095_s_at	LIM and senescent cell antigen-like domains 3	LIMS3	96626	3
209122_at	adipose differentiation-related protein	ADFP	123	3

APPENDIX C: Genes downregulated in AAA vs. AOD (continued).

Probe	Gene Description	Gene Symbol	Entrez Gene ID	Fold Change
228863_at	Protocadherin 17	PCDH17	27253	3
209921_at	solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	SLC7A11	23657	3
1569603_at	SH3-domain GRB2-like (endophilin) interacting protein 1	DKFZp761D221	84251	3
206026_s_at	tumor necrosis factor, alpha-induced protein 6	TNFAIP6	7130	3
208161_s_at	ATP-binding cassette, sub-family C (CFTR/MRP), member 3	ABCC3	8714	3
202311_s_at	collagen, type I, alpha 1	COL1A1	1277	3
219915_s_at	solute carrier family 16 (monocarboxylic acid transporters), member 10	SLC16A10	117247	3
202834_at	angiotensinogen (serpin peptidase inhibitor, clade A, member 8)	AGT	183	3
202998_s_at	lysyl oxidase-like 2	LOXL2	4017	3
221577_x_at	growth differentiation factor 15	GDF15	9518	3
239443_at	protocadherin beta 6	PCDHB6	56130	3
202087_s_at	cathepsin L	CTSL	1514	3
210305_at	phosphodiesterase 4D interacting protein (myomegalin)	PDE4DIP	9659	3
241872_at	SH3-domain GRB2-like (endophilin) interacting protein 1	DKFZp761D221	84251	3
209960_at	hepatocyte growth factor (hepapoietin A; scatter factor)	HGF	3082	3
229139_at	junctophilin 1	JPH1	56704	3
236121_at	olfactory receptor, family 51, subfamily E, member 2	OR51E2	81285	3
208475_at	FERM domain containing 4A	FRMD4A	55691	3
217678_at	solute carrier family 7, (cationic amino acid transporter, y+ system) member 11	SLC7A11	23657	3
224324_at	maestro ; maestro	MRO	83876	3
224657_at	ERBB receptor feedback inhibitor 1	ERRFI1	54206	3
205450_at	phosphorylase kinase, alpha 1 (muscle)	PHKA1	5255	3
205567_at	carbohydrate (keratan sulfate Gal-6) sulfotransferase 1	CHST1	8534	3
229876_at	Phosphorylase kinase, alpha 1 (muscle)	PHKA1	5255	3

APPENDIX C: Genes downregulated in AAA vs. AOD (continued).

Probe	Gene Description	Gene Symbol	Entrez Gene ID	Fold Change
238289_at	Retinitis pigmentosa GTPase regulator	RPGR	6103	3
232530_at	phospholipase D1, phophatidylcholine-specific	PLD1	5337	3
1566129_at	LIM and senescent cell antigen-like domains 1	LIMS1	3987	3
202208_s_at	ADP-ribosylation factor-like 7	ARL7	10123	3
203823_at	regulator of G-protein signalling 3	RGS3	5998	3
210755_at	hepatocyte growth factor (hepapoietin A; scatter factor)	HGF	3082	3
201468_s_at	NAD(P)H dehydrogenase, quinone 1	NQO1	1728	3
215761_at	Dmx-like 2	DMXL2	23312	3
209882_at	Ras-like without CAAX 1	RIT1	6016	3
202856_s_at	solute carrier family 16 (monocarboxylic acid transporters), member 3	SLC16A3	9123	3
230748_at	solute carrier family 16 (monocarboxylic acid transporters), member 6	SLC16A6	440459	3
204163_at	elastin microfibril interfacer 1	EMILIN1	11117	3
203382_s_at	apolipoprotein E	APOE	348	3
200648_s_at	glutamate-ammonia ligase (glutamine synthetase)	GLUL	2752	2
207224_s_at	sialic acid binding Ig-like lectin 7	SIGLEC7	27036	2
235629_at	Fibronectin 1	FN1	2335	2
217430_x_at	collagen, type I, alpha 1	COL1A1	1277	2
160020_at	matrix metallopeptidase 14 (membrane-inserted)	MMP14	4323	2
226814_at	ADAM metallopeptidase with thrombospondin type 1 motif, 9	ADAMTS9	56999	2
233167_at	selenoprotein O	SELO	83642	2
212013_at	peroxidasin homolog (Drosophila)	PXDN	7837	2
207837_at	RNA binding protein with multiple splicing	RBPMS	11030	2
223567_at	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6B	SEMA6B	10501	2
1558460_at	ATP-binding cassette, sub-family C (CFTR/MRP), member 5	ABCC5	10057	2
237624_at	Collagen, type IV, alpha 2	COL4A2	1284	2

APPENDIX C: Genes downregulated in AAA vs. AOD (continued).

Probe	Gene Description	Gene Symbol	Entrez Gene ID	Fold Change
218113_at	transmembrane protein 2	TMEM2	23670	2
35666_at	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3F	SEMA3F	6405	2
210612_s_at	synaptojanin 2	SYNJ2	8871	2
213592_at	angiotensin II receptor-like 1	AGTRL1	187	2
1569157_s_at	hypothetical protein LOC162993	LOC162993	162993	2
201261_x_at	biglycan	BGN	633	2
203325_s_at	collagen, type V, alpha 1	COL5A1	1289	2
213506_at	coagulation factor II (thrombin) receptor-like 1	F2RL1	2150	2
223683_at	zinc finger, MYND-type containing 15	ZMYND15	84225	2
202627_s_at	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	SERPINE1	5054	2
236910_at	Mitochondrial ribosomal protein L39	MRPL39	54148	2
220750_s_at	leucine proline-enriched proteoglycan (leprecan) 1	LEPRE1	64175	2
223251_s_at	ankyrin repeat domain 10	ANKRD10	55608	2
221730_at	collagen, type V, alpha 2	COL5A2	1290	2
202974_at	membrane protein, palmitoylated 1, 55kDa	MPP1	4354	2
205936_s_at	hexokinase 3 (white cell)	HK3	3101	2
205180_s_at	ADAM metallopeptidase domain 8 ; ADAM metallopeptidase domain 8	ADAM8	101	2
227289_at	hypothetical protein LOC144997	LOC144997	144997	2
219394_at	phosphatidylglycerophosphate synthase	PGS1	9489	2
212828_at	synaptojanin 2	SYNJ2	8871	2
236545_at	Protein phosphatase 3 (formerly 2B), catalytic subunit, alpha isoform (calcineurin A alpha)	PPP3CA	5530	2
209135_at	aspartate beta-hydroxylase	ASPH	444	2
218451_at	CUB domain containing protein 1	CDCP1	64866	2

APPENDIX C: Genes downregulated in AAA vs. AOD (continued).

Probe	Gene Description	Gene Symbol	Entrez Gene ID	Fold Change
212488_at	collagen, type V, alpha 1	COL5A1	1289	2
209365_s_at	extracellular matrix protein 1	ECM1	1893	2
228816_at	hypothetical protein LOC92270	LOC92270	92270	2
212658_at	lipoma HMGIC fusion partner-like 2	LHFPL2	10184	2
241384_x_at	hypothetical protein MGC40579	MGC40579	256356	2
238542_at	UL16 binding protein 2	ULBP2	80328	2
229218_at	Collagen, type I, alpha 2	COL1A2	1278	2
222446_s_at	beta-site APP-cleaving enzyme 2	BACE2	25825	2
224773_at	neuron navigator 1	NAV1	89796	2
212012_at	peroxidasin homolog (Drosophila)	PXDN	7837	2
61734_at	reticulocalbin 3, EF-hand calcium binding domain	RCN3	57333	2
202862_at	fumarylacetoacetate hydrolase (fumarylacetoacetase)	FAH	2184	2
227314_at	Integrin, alpha 2 (CD49B, alpha 2 subunit of VLA-2 receptor)	ITGA2	3673	2
205099_s_at	chemokine (C-C motif) receptor 1	CCR1	1230	2
1568765_at	serpin peptidase inhibitor, clade E (nexin, plasminogen activator inhibitor type 1), member 1	SERPINE1	5054	2
207135_at	5-hydroxytryptamine (serotonin) receptor 2A	HTR2A	3356	2
219815_at	galactose-3-O-sulfotransferase 4	GAL3ST4	79690	2
205574_x_at	bone morphogenetic protein 1	BMP1	649	2
202855_s_at	solute carrier family 16 (monocarboxylic acid transporters), member 3	SLC16A3	9123	2
236153_at	Suppressor of hairy wing homolog 4 (Drosophila)	SUHW4	54816	2
219957_at	RUN and FYVE domain containing 2	RUFY2	55680	2
232685_at	Ets variant gene 6 (TEL oncogene)	ETV6	2120	2
203417_at	microfibrillar-associated protein 2	MFAP2	4237	2
237411_at	ADAM metallopeptidase with thrombospondin type 1 motif, 6	ADAMTS6	11174	2
206298_at	Rho GTPase activating protein 22	ARHGAP22	58504	2

APPENDIX C: Genes downregulated in AAA vs. AOD (continued).

Probe	Gene Description	Gene Symbol	Entrez Gene ID	Fold Change
218585_s_at	denticleless homolog (Drosophila)	DTL	51514	2
207714_s_at	serpin peptidase inhibitor, clade H (heat shock protein 47), member 1, (collagen binding protein 1)	SERPINH1	871	2
226722_at	family with sequence similarity 20, member C	FAM20C	56975	2
205572_at	angiopoietin 2	ANGPT2	285	2
214702_at	fibronectin 1	FN1	2335	2
203282_at	glucan (1,4-alpha-), branching enzyme 1	GBE1	2632	2
209053_s_at	Wolf-Hirschhorn syndrome candidate 1	WHSC1	7468	2
217867_x_at	beta-site APP-cleaving enzyme 2	BACE2	25825	2
217788_s_at	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2	GALNT2	2590	2
1559814_at	Chondroitin sulfate synthase 3	CSS3	337876	2
1556151_at	T-cell immunomodulatory protein	CDA08	81533	2
200827_at	procollagen-lysine 1, 2-oxoglutarate 5-dioxygenase 1	PLOD1	5351	2
221143_at	replication protein A4, 34kDa	RPA4	29935	2
1558078_at	DNA directed RNA polymerase II polypeptide J-related gene	POLR2J2	246721	2
210422_x_at	solute carrier family 11 (proton-coupled divalent metal ion transporters), member 1	SLC11A1	6556	2
228054_at	transmembrane protein 44	TMEM44	93109	2
219102_at	reticulocalbin 3, EF-hand calcium binding domain	RCN3	57333	2
201505_at	laminin, beta 1	LAMB1	3912	2
233090_at	Glypican 6	GPC6	10082	2
217518_at	fer-1-like 3, myoferlin (C. elegans)	FER1L3	26509	2
219457_s_at	Ras and Rab interactor 3	RIN3	79890	2
200840_at	lysyl-tRNA synthetase	KARS	3735	2
208928_at	P450 (cytochrome) oxidoreductase	POR	5447	2

APPENDIX C: Genes downregulated in AAA vs. AOD (continued).

Probe	Gene Description	Gene Symbol	Entrez Gene ID	Fold Change
204150_at	stabilin 1	STAB1	23166	2
205525_at	caldesmon 1	CALD1	800	2
210119_at	potassium inwardly-rectifying channel, subfamily J, member 15	KCNJ15	3772	2
213943_at	twist homolog 1 (acrocephalosyndactyly 3; Saethre-Chotzen syndrome) (Drosophila)	TWIST1	7291	2
201655_s_at	heparan sulfate proteoglycan 2 (perlecan)	HSPG2	3339	2
218749_s_at	solute carrier family 24 (sodium/potassium/calcium exchanger), member 6	SLC24A6	80024	2
236249_at	IKK interacting protein	IKIP	121457	2
202733_at	procollagen-proline, 2-oxoglutarate 4-dioxygenase (proline 4-hydroxylase), alpha polypeptide II	P4HA2	8974	2
208613_s_at	filamin B, beta (actin binding protein 278)	FLNB	2317	2
213001_at	angiopoietin-like 2	ANGPTL2	23452	2
205676_at	cytochrome P450, family 27, subfamily B, polypeptide 1	CYP27B1	1594	2
231823_s_at	KIAA1295	KIAA1295	285590	2
236475_at	Microtubule associated monoxygenase, calponin and LIM domain containing 2	MICAL2	9645	2
209397_at	malic enzyme 2, NAD(+)-dependent, mitochondrial	ME2	4200	2
220668_s_at	DNA (cytosine-5-)-methyltransferase 3 beta	DNMT3B	1789	2
1562416_at	Filamin B, beta (actin binding protein 278)	FLNB	2317	2
206028_s_at	c-mer proto-oncogene tyrosine kinase	MERTK	10461	2
228845_at	hypothetical protein LOC196463	LOC196463	196463	2
210868_s_at	ELOVL family member 6, elongation of long chain fatty acids (FEN1/Elo2, SUR4/Elo3-like, yeast)	ELOVL6	79071	2
203925_at	glutamate-cysteine ligase, modifier subunit	GCLM	2730	2
229899_s_at	similar to RPE-spondin	HSUP1	441951	2

APPENDIX C: Genes downregulated in AAA vs. AOD (continued).

Probe	Gene Description	Gene Symbol	Entrez Gene ID	Fold Change
214435_x_at	v-ral simian leukemia viral oncogene homolog A (ras related)	RALA	5898	2
209172_s_at	centromere protein F, 350/400ka (mitosin) ; centromere protein F, 350/400ka (mitosin)	CENPF	1063	2
209803_s_at	pleckstrin homology-like domain, family A, member 2	PHLDA2	7262	2
218502_s_at	trichorhinophalangeal syndrome I	TRPS1	7227	2
221729_at	collagen, type V, alpha 2	COL5A2	1290	2
202202_s_at	laminin, alpha 4	LAMA4	3910	2
228520_s_at	Amyloid beta (A4) precursor-like protein 2	APLP2	334	2
208002_s_at	acyl-CoA thioesterase 7	ACOT7	11332	2
215198_s_at	caldesmon 1	CALD1	800	2
226216_at	Insulin receptor	INSR	3643	2
232080_at	HECT, C2 and WW domain containing E3 ubiquitin protein ligase 2	HECW2	57520	2
210184_at	integrin, alpha X (antigen CD11C (p150), alpha polypeptide)	ITGAX	3687	2
213700_s_at	Pyruvate kinase, muscle	PKM2	5315	2
239719_at	CD109 antigen (Gov platelet alloantigens)	CD109	135228	2
243305_at	Kelch domain containing 5	KIAA1340	57542	2
213905_x_at	biglycan ; serologically defined colon cancer antigen 33	BGN	10194	2
218815_s_at	transmembrane protein 51	TMEM51	55092	2
204114_at	nidogen 2 (osteonidogen)	NID2	22795	2
219952_s_at	mucolipin 1	MCOLN1	57192	2
214052_x_at	BAT2 domain containing 1	XTP2	23215	2
222680_s_at	denticleless homolog (Drosophila)	DTL	51514	2
203903_s_at	hephaestin	HEPH	9843	2
207828_s_at	centromere protein F, 350/400ka (mitosin)	CENPF	1063	2
226498_at	(vascular endothelial growth factor/vascular permeability factor receptor)	FLT1	2321	2
234372_at	Family with sequence similarity 70, member B	MGC20579	348013	2

Appendix D: Genes upregulated in AAA vs. NA

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
215565_at	dystrobrevin, beta	DTNB	1838	88
216984_x_at	Immunoglobulin lambda joining 3	IGLC2	3538	79
217378_x_at	similar to Ig kappa chain precursor V region (orphon V108) - human (fragment)	LOC391427	391427	62
235401_s_at	Fc receptor-like and mucin-like 1	FCRLM1	84824	58
211643_x_at	Immunoglobulin kappa variable 1-5	IGKC	3514	55
234884_x_at	Immunoglobulin lambda joining 3	IGLC2	3538	53
215214_at	immunoglobulin lambda variable 3-25	IGLV3-25	28793	52
215946_x_at	similar to omega protein	LOC91353	91353	50
215949_x_at	immunoglobulin heavy constant mu	IGHM	3507	50
211644_x_at	immunoglobulin kappa constant	IGKC	3514	47
230896_at	coiled-coil domain containing 4	CCDC4	389206	47
217148_x_at	immunoglobulin lambda variable 2-14	IGLV2-14	28815	42
235982_at	Fc receptor-like 1	FCRL1	115350	39
228518_at	immunoglobulin heavy constant gamma 1 (G1m marker)	IGHG1	3500	38
205049_s_at	CD79A antigen (immunoglobulin-associated alpha)	CD79A	973	36
217480_x_at	similar to Ig kappa chain	LOC339562	339562	34
216207_x_at	immunoglobulin kappa variable 1D-13	IGKV1D-13	28902	29
1563217_at	Protein kinase (cAMP-dependent, catalytic) inhibitor alpha	PKIA	5569	21
230673_at	polycystic kidney and hepatic disease 1 (autosomal recessive)-like 1	PKHD1L1	93035	21
212592_at	Immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	IGJ	3512	20
234306_s_at	SLAM family member 7	SLAMF7	57823	19
220059_at	BCR downstream signaling 1	BRDG1	26228	17
216542_x_at	immunoglobulin heavy constant gamma 1 (G1m marker) ; hypothetical protein MGC27165	IGHG1	283650 ; 3500	16
224022_x_at	wingless-type MMTV integration site family, member 16	WNT16	51384	15
206135_at	suppression of tumorigenicity 18 (breast carcinoma) (zinc finger protein)	ST18	9705	15

Appendix D: Genes upregulated in AAA vs.NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
227300_at	hypothetical protein LOC338773	LOC338773	338773	15
242388_x_at	T-cell activation GTPase activating protein	TAGAP	117289	15
206398_s_at	CD19 antigen	CD19	930	15
206914_at	class-I MHC-restricted T cell associated molecule	CRTAM	56253	14
221602_s_at	Fas apoptotic inhibitory molecule 3 ; Fas apoptotic inhibitory molecule 3	FAIM3	9214	13
244887_at	Regulator of G-protein signalling 13	RGS13	6003	13
237009_at	CD69 antigen (p60, early T-cell activation antigen)	CD69	969	12
211062_s_at	Carbopeptidase Z	CPZ	8532	12
220338_at	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	55103	12
235965_at	DKFZP434B0335 protein	DKFZP434	25851	12
219667_s_at	B-cell scaffold protein with ankyrin repeats 1	BANK1	55024	11
229723_at	T-cell activation GTPase activating protein	TAGAP	117289	11
223484_at	normal mucosa of esophagus specific 1	NMES1	84419	11
234050_at	T-cell activation GTPase activating protein	TAGAP	117289	11
206150_at	tumor necrosis factor receptor superfamily, member 7	TNFRSF7	939	11
236293_at	Ras homolog gene family, member H	RHOH	399	11
224406_s_at	Fc receptor-like 5 ; Fc receptor-like 5	FCRL5	83416	11
221969_at	Paired box gene 5 (B-cell lineage specific activator)	PAX5	5079	11
1563674_at	Fc receptor-like 2	FCRL2	79368	10
209606_at	pleckstrin homology, Sec7 and coiled-coil domains, binding protein	PSCDBP	9595	10
236341_at	cytotoxic T-lymphocyte-associated protein 4	CTLA4	1493	10
244357_at	Stromal membrane-associated protein 1-like	LOC64744	64744	10
221601_s_at	Fas apoptotic inhibitory molecule 3 ; Fas apoptotic inhibitory molecule 3	FAIM3	9214	10
1554474_a_at	monooxygenase, DBH-like 1	MOXD1	26002	10
205692_s_at	CD38 antigen (p45)	CD38	952	10

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
222106_at	prion protein 2 (dublet)	PRND	23627	10
1569225_a_at	sex comb on midleg-like 4 (Drosophila)	SCML4	256380	10
202988_s_at	regulator of G-protein signalling 1	RGS1	5996	9
227224_at	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	55103	9
239237_at	Amphiphysin (Stiff-Man syndrome with breast cancer 128kDa autoantigen)	AMPH	273	9
228658_at	hypothetical protein LOC150271	LOC150271	150271	9
203798_s_at	visinin-like 1	VSNL1	7447	9
206804_at	CD3G antigen, gamma polypeptide (TiT3 complex)	CD3G	917	9
205990_s_at	wingless-type MMTV integration site family, member 5A	WNT5A	7474	9
207734_at	lymphocyte transmembrane adaptor 1	LAX1	54900	9
1552542_s_at	T-cell activation GTPase activating protein	TAGAP	117289	9
1559170_at	Similar to ankyrin repeat domain 20A ; Hypothetical gene supported by NM_032250		388466	9
227361_at	heparan sulfate (glucosamine) 3-O-sulfotransferase 3B1	HS3ST3B1	9953	9
205671_s_at	major histocompatibility complex, class II, DO beta	HLA-DOB	3112	9
228964_at	PR domain containing 1, with ZNF domain	PRDM1	639	9
34210_at	CD52 antigen (CAMPATH-1 antigen)	CD52	1043	9
224009_x_at	dehydrogenase/reductase (SDR family) member 9	DHRS9	10170	9
1558662_s_at	B-cell scaffold protein with ankyrin repeats 1	BANK1	55024	9
220068_at	pre-B lymphocyte gene 3	VPREB3	29802	9
1552343_s_at	phosphodiesterase 7A	PDE7A	5150	8
224402_s_at	Fc receptor-like 4	FCRL4	83417	8
206337_at	chemokine (C-C motif) receptor 7	CCR7	1236	8
219463_at	chromosome 20 open reading frame 103	C20orf103	24141	8
204052_s_at	secreted frizzled-related protein 4	SFRP4	6424	8
222895_s_at	B-cell CLL/lymphoma 11B (zinc finger protein)	BCL11B	64919	8

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
217028_at	chemokine (C-X-C motif) receptor 4	CXCR4	7852	8
210164_at	granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	GZMB	3002	8
211919_s_at	chemokine (C-X-C motif) receptor 4	CXCR4	7852	8
1558972_s_at	chromosome 6 open reading frame 190	C6orf190	387357	8
203936_s_at	matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	MMP9	4318	8
204661_at	CD52 antigen (CAMPATH-1 antigen) ; CD52 antigen (CAMPATH-1 antigen)	CD52	1043	8
242104_at	Ankyrin repeat and KH domain containing 1	ANKHD1	54882	8
204951_at	ras homolog gene family, member H	RHOH	399	8
1553856_s_at	purinergic receptor P2Y, G-protein coupled, 10	P2RY10	27334	8
1557285_at	Amphiregulin (schwannoma-derived growth factor)	AREG	374	8
222915_s_at	B-cell scaffold protein with ankyrin repeats 1	BANK1	55024	8
244261_at	interleukin 28 receptor, alpha (interferon, lambda receptor)	IL28RA	163702	8
1559263_s_at	zinc finger CCCH-type containing 12D	ZC3H12D	340152	8
209596_at	matrix-remodelling associated 5	MXRA5	25878	8
223750_s_at	toll-like receptor 10	TLR10	81793	8
206834_at	hemoglobin, delta ; hemoglobin, delta	HBD	3045	8
226218_at	Interleukin 7 receptor	IL7R	3575	8
227566_at	neurotrimin	HNT	50863	7
215967_s_at	lymphocyte antigen 9	LY9	4063	7
241891_at	Dedicator of cytokinesis 8	DOCK8	81704	7
205114_s_at	chemokine (C-C motif) ligand 3	CCL3	414062	7
1405_i_at	chemokine (C-C motif) ligand 5	CCL5	6352	7
204286_s_at	phorbol-12-myristate-13-acetate-induced protein 1	PMAIP1	5366	7
242947_at	DnaJ (Hsp40) homolog, subfamily C, member 16	KIAA0962	23341	7
212311_at	KIAA0746 protein	KIAA0746	23231	7

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
242458_at	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	55103	7
216834_at	regulator of G-protein signalling 1	RGS1	5996	7
202901_x_at	cathepsin S	CTSS	1520	7
205590_at	RAS guanyl releasing protein 1 (calcium and DAG-regulated)	RASGRP1	10125	7
209670_at	T cell receptor alpha constant ; T cell receptor alpha constant	TRAC	28755	7
230983_at	B-cell novel protein 1	BCNP1	199786	7
209708_at	monooxygenase, DBH-like 1	MOXD1	26002	7
213425_at	wingless-type MMTV integration site family, member 5A	WNT5A	7474	7
1568604_a_at	Ca2+-dependent secretion activator	CADPS	8618	7
209201_x_at	chemokine (C-X-C motif) receptor 4	CXCR4	7852	7
221266_s_at	transmembrane 7 superfamily member 4 ; transmembrane 7 superfamily member 4	TM7SF4	81501	7
228377_at	kelch-like 14 (Drosophila)	KLHL14	57565	7
235372_at	Fc receptor-like and mucin-like 1	FCRLM1	84824	7
237496_at	3'-phosphoadenosine 5'-phosphosulfate synthase 2	PAPSS2	9060	7
207031_at	bagpipe homeobox homolog 1 (Drosophila)	BAPX1	579	7
227533_at	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	55103	7
235353_at	KIAA0746 protein	KIAA0746	23231	6
228167_at	kelch-like 6 (Drosophila)	KLHL6	89857	6
209138_x_at	Immunoglobulin lambda joining 3	IGLC2	3538	6
226811_at	family with sequence similarity 46, member C	FAM46C	54855	6
220169_at	hypothetical protein FLJ23235	FLJ23235	80008	6
202643_s_at	tumor necrosis factor, alpha-induced protein 3	TNFAIP3	7128	6
209671_x_at	T cell receptor alpha locus	TRA@	28755	6
205484_at	signaling threshold regulating transmembrane adaptor 1	SIT1	27240	6

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
226435_at	papilin, proteoglycan-like sulfated glycoprotein	PAPLN	89932	6
1554343_a_at	BCR downstream signaling 1	BRDG1	26228	6
205249_at	early growth response 2 (Krox-20 homolog, Drosophila)	EGR2	1959	6
210354_at	interferon, gamma	IFNG	3458	6
219734_at	SID1 transmembrane family, member 1	SIDT1	54847	6
206513_at	absent in melanoma 2	AIM2	9447	6
219799_s_at	dehydrogenase/reductase (SDR family) member 9	DHRS9	10170	6
227189_at	copine V	CPNE5	57699	6
228258_at	TBC1 domain family, member 10C	TBC1D10C	374403	6
225792_at	Hook homolog 1 (Drosophila)	HOOK1	51361	6
211796_s_at	T cell receptor beta variable 21-1	TRBV21-1	28566	6
214615_at	purinergic receptor P2Y, G-protein coupled, 10	P2RY10	27334	6
221558_s_at	lymphoid enhancer-binding factor 1	LEF1	51176	6
205419_at	Epstein-Barr virus induced gene 2 (lymphocyte-specific G protein-coupled receptor)	EBI2	1880	6
211597_s_at	homeodomain-only protein ; homeodomain-only protein	HOP	84525	6
211902_x_at	T cell receptor alpha locus	TRA@	6955	6
212314_at	KIAA0746 protein	KIAA0746	23231	6
235885_at	purinergic receptor P2Y, G-protein coupled, 12	P2RY12	64805	6
207777_s_at	SP140 nuclear body protein	SP140	11262	6
214405_at	CUG triplet repeat, RNA binding protein 2	CUGBP2	10659	6
233302_at	B-cell CLL/lymphoma 11B (zinc finger protein)	BCL11B	64919	5
219454_at	EGF-like-domain, multiple 6	EGFL6	25975	5
227134_at	synaptotagmin-like 1	SYTL1	84958	5
205828_at	matrix metallopeptidase 3	MMP3	4314	5
230753_at	similar to RIKEN cDNA 4930424G05	LOC197135	197135	5

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
209829_at	chromosome 6 open reading frame 32	C6orf32	9750	5
210915_x_at	T cell receptor beta variable 19 ; T cell receptor beta constant 1	TRBV19	28568	5
207979_s_at	CD8 antigen, beta polypeptide 1 (p37)	CD8B1	926	5
218858_at	DEP domain containing 6	DEPDC6	64798	5
205648_at	wingless-type MMTV integration site family member 2	WNT2	7472	5
219985_at	heparan sulfate (glucosamine) 3-O-sulfotransferase 3A1	HS3ST3A1	9955	5
39318_at	T-cell leukemia/lymphoma 1A	TCL1A	8115	5
204103_at	chemokine (C-C motif) ligand 4	CCL4	6351	5
232112_at	Ral GEF with PH domain and SH3 binding motif 2	RALGPS2	55103	5
230233_at	RasGEF domain family, member 1B	RASGEF1B	153020	5
232739_at	Spi-B transcription factor (Spi-1/PU.1 related)	SPIB	6689	5
241871_at	calcium/calmodulin-dependent protein kinase IV	CAMK4	814	5
221331_x_at	cytotoxic T-lymphocyte-associated protein 4	CTLA4	1493	5
1570585_at	hypothetical protein LOC196264	LOC196264	196264	5
220577_at	GTPase, very large interferon inducible 1	GVIN1	387751	5
1555613_a_at	zeta-chain (TCR) associated protein kinase 70kDa	ZAP70	7535	5
232277_at	Solute carrier family 28 (sodium-coupled nucleoside transporter), member 3	SLC28A3	64078	5
208268_at	ADAM metallopeptidase domain 28	ADAM28	10863	5
205831_at	CD2 antigen (p50), sheep red blood cell receptor ; CD2 antigen (p50), sheep red blood cell receptor	CD2	914	5
1560999_a_at	Interleukin 12 receptor, beta 2	IL12RB2	3595	5
204007_at	Fc fragment of IgG, low affinity IIIb, receptor (CD16b)	FCGR3B	2215	5
1553155_x_at	ATPase, H+ transporting, lysosomal 38kDa, V0 subunit d isoform 2	ATP6V0D2	245972	5
230011_at	similar to mouse meiosis defective 1 gene	MGC40042	150365	5
210279_at	G protein-coupled receptor 18	GPR18	2841	5

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
1560396_at	Kelch-like 6 (Drosophila)	KLHL6	89857	5
211742_s_at	ecotropic viral integration site 2B ; ecotropic viral integration site 2B	EVI2B	2124	5
242946_at	CD53 antigen	CD53	963	5
204563_at	selectin L (lymphocyte adhesion molecule 1)	SELL	6402	5
220005_at	purinergic receptor P2Y, G-protein coupled, 13	P2RY13	53829	5
204116_at	interleukin 2 receptor, gamma (severe combined immunodeficiency)	IL2RG	3561	5
236539_at	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	PTPN22	26191	5
229695_at	Chromosome 10 open reading frame 45	C10orf45	83641	5
1560416_at	dynein, axonemal, heavy polypeptide 11	DNAH11	8701	5
243981_at	serine/threonine kinase 4	STK4	6789	5
205666_at	flavin containing monooxygenase 1	FMO1	2326	5
204891_s_at	lymphocyte-specific protein tyrosine kinase	LCK	3932	5
213958_at	CD6 antigen ; CD6 antigen	CD6	923	5
219117_s_at	FK506 binding protein 11, 19 kDa	FKBP11	51303	5
219528_s_at	B-cell CLL/lymphoma 11B (zinc finger protein)	BCL11B	64919	5
206404_at	fibroblast growth factor 9 (glia-activating factor)	FGF9	2254	5
202902_s_at	cathepsin S	CTSS	1520	5
223729_at	cat eye syndrome chromosome region, candidate 2	CECR2	27443	5
204051_s_at	secreted frizzled-related protein 4	SFRP4	6424	5
219874_at	solute carrier family 12 (potassium/chloride transporters), member 8	SLC12A8	84561	5
206773_at	lymphocyte antigen 6 complex, locus H	LY6H	4062	5
239529_at	chromosome 5 open reading frame 20	C5orf20	140947	5
213502_x_at	similar to bK246H3.1 (immunoglobulin lambda-like polypeptide 1, pre-B-cell specific)	LOC91316	91316	5
202644_s_at	tumor necrosis factor, alpha-induced protein 3	TNFAIP3	7128	5
1563473_at	Protein phosphatase 1, regulatory (inhibitor) subunit 16B	PPP1R16B	26051	5

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
1554208_at	similar to mouse meiosis defective 1 gene	MGC40042	150365	5
222859_s_at	dual adaptor of phosphotyrosine and 3-phosphoinositides	DAPP1	27071	5
219648_at	dilute suppressor	DSU	55686	5
232824_at	ATPase, Class II, type 9B	ATP9B	374868	5
229686_at	purinergic receptor P2Y, G-protein coupled, 8	P2RY8	286530	5
230261_at	ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 4	ST8SIA4	7903	5
1552899_at	hypothetical protein MGC34034	MGC34034	154089	5
213539_at	CD3D antigen, delta polypeptide (TiT3 complex)	CD3D	915	5
220035_at	nucleoporin 210kDa	NUP210	23225	4
216748_at	pyrin and HIN domain family, member 1	PYHIN1	149628	4
205997_at	ADAM metallopeptidase domain 28	ADAM28	10863	4
214084_x_at	neutrophil cytosolic factor 1 (47kDa, chronic granulomatous disease, autosomal 1)	NCF1	4687	4
203917_at	coxsackie virus and adenovirus receptor	CXADR	1525	4
219812_at	hypothetical protein MGC2463	MGC2463	79037	4
1552480_s_at	protein tyrosine phosphatase, receptor type, C	PTPRC	5788	4
241860_at	Serine/threonine kinase 17b (apoptosis-inducing)	STK17B	9262	4
232383_at	transcription factor EC	TFEC	22797	4
211339_s_at	IL2-inducible T-cell kinase	ITK	3702	4
222020_s_at	neurotrimin	HNT	50863	4
230493_at	transmembrane protein 46	TMEM46	387914	4
214470_at	killer cell lectin-like receptor subfamily B, member 1	KLRB1	3820	4
210116_at	SH2 domain protein 1A, Duncan's disease (lymphoproliferative syndrome)	SH2D1A	4068	4
211771_s_at	POU domain, class 2, transcription factor 2 ; POU domain, class 2, transcription factor 2	POU2F2	5452	4
231377_at	similar to Ab2-183	LOC158830	158830	4
207651_at	G protein-coupled receptor 171	GPR171	29909	4

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
206100_at	carboxypeptidase M	CPM	1368	4
1554676_at	proteoglycan 1, secretory granule	PRG1	5552	4
228636_at	basic helix-loop-helix domain containing, class B, 5	BHLHB5	27319	4
209763_at	chordin-like 1	CHRDL1	91851	4
243109_at	Multiple C2-domains with two transmembrane regions 2	MCTP2	55784	4
1554240_a_at	integrin, alpha L (antigen CD11A (p180)	ITGAL	3683	4
211478_s_at	dipeptidylpeptidase 4 (CD26, adenosine deaminase complexing protein 2)	DPP4	1803	4
232311_at	Beta-2-microglobulin	B2M	567	4
236738_at	Similar to LOC166075	LOC401097	401097	4
201341_at	ectodermal-neural cortex (with BTB-like domain)	ENC1	8507	4
236295_s_at	NOD3 protein	NOD3	197358	4
210347_s_at	B-cell CLL/lymphoma 11A (zinc finger protein)	BCL11A	53335	4
1555372_at	BCL2-like 11 (apoptosis facilitator)	BCL2L11	10018	4
232843_s_at	dedicator of cytokinesis 8	DOCK8	81704	4
215468_at	DEAH (Asp-Glu-Ala-His) box polypeptide 9	DHX9	1660	4
213764_s_at	microfibrillar associated protein 5	MFAP5	8076	4
233514_x_at	testis expressed sequence 11	TEX11	56159	4
211745_x_at	hemoglobin, alpha 1 ; hemoglobin, alpha 1 ; hemoglobin, alpha 2 ; hemoglobin, alpha 2	HBA1 ; HBA2	3039 ; 3040	4
211696_x_at	hemoglobin, beta ; hemoglobin, beta	HBB	3043	4
225912_at	tumor protein p53 inducible nuclear protein 1	TP53INP1	94241	4
207001_x_at	TSC22 domain family, member 3	TSC22D3	1831	4
212588_at	protein tyrosine phosphatase, receptor type, C	PTPRC	5788	4
35974_at	lymphoid-restricted membrane protein	LRMP	4033	4
214203_s_at	proline dehydrogenase (oxidase) 1	PRODH	5625	4
244813_at	RAD51-like 1 (S. cerevisiae)	RAD51L1	5890	4

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
243006_at	FYN oncogene related to SRC, FGR, YES	FYN	2534	4
1559078_at	B-cell CLL/lymphoma 11A (zinc finger protein)	BCL11A	53335	4
203413_at	NEL-like 2 (chicken) ; NEL-like 2 (chicken)	NELL2	4753	4
228335_at	claudin 11 (oligodendrocyte transmembrane protein)	CLDN11	5010	4
204198_s_at	runt-related transcription factor 3	RUNX3	864	4
203397_s_at	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 3 (GalNAc-T3)	GALNT3	2591	4
236471_at	nuclear factor (erythroid-derived 2)-like 3	NFE2L3	9603	4
232231_at	runt-related transcription factor 2	RUNX2	860	4
214012_at	type 1 tumor necrosis factor receptor shedding aminopeptidase regulator	ARTS-1	51752	4
236995_x_at	transcription factor EC	TFEC	22797	4
223746_at	serine/threonine kinase 4	STK4	6789	4
243683_at	Mortality factor 4 like 2	MORF4L2	9643	4
222717_at	serum deprivation response (phosphatidylserine binding protein)	SDPR	8436	4
210258_at	regulator of G-protein signalling 13	RGS13	6003	4
207339_s_at	lymphotoxin beta (TNF superfamily, member 3)	LTB	4050	4
205943_at	tryptophan 2,3-dioxygenase	TDO2	6999	4
214070_s_at	ATPase, Class V, type 10B	ATP10B	23120	4
227210_at	Scm-like with four mbt domains 2	SFMBT2	57713	4
1566887_x_at	KIAA0284	KIAA0284	283638	4
242109_at	T-complex-associated-testis-expressed 1-like 1	TCTEL1	6993	4
207655_s_at	B-cell linker	BLNK	29760	4
204205_at	apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G	APOBEC3G	60489	4
209827_s_at	interleukin 16 (lymphocyte chemoattractant factor)	IL16	3603	4
1552386_at	hypothetical protein FLJ33641	FLJ33641	202309	4
212587_s_at	protein tyrosine phosphatase, receptor type, C	PTPRC	5788	4

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
223423_at	G protein-coupled receptor 160	GPR160	26996	4
228343_at	POU domain, class 2, transcription factor 2	POU2F2	5452	4
1552398_a_at	C-type lectin domain family 12, member A	CLEC12A	160364	4
237361_at	Doublecortin and CaM kinase-like 1	DCAMKL1	9201	4
232617_at	cathepsin S	CTSS	1520	4
206060_s_at	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	PTPN22	26191	4
219551_at	ELL associated factor 2	EAF2	55840	4
203932_at	major histocompatibility complex, class II, DM beta	HLA-DMB	3109	4
211795_s_at	FYN binding protein (FYB-120/130)	FYB	2533	4
40665_at	flavin containing monooxygenase 3	FMO3	2328	4
220918_at	chromosome 21 open reading frame 96	C21orf96	80215	4
207238_s_at	protein tyrosine phosphatase, receptor type, C	PTPRC	5788	4
1552626_a_at	hypothetical protein DKFZp566N034	DKFZP	81615	4
204118_at	CD48 antigen (B-cell membrane protein) ; CD48 antigen (B-cell membrane protein)	CD48	962	4
206171_at	adenosine A3 receptor	ADORA3	140	4
220252_x_at	chromosome X open reading frame 21	CXorf21	80231	4
204674_at	lymphoid-restricted membrane protein	LRMP	4033	4
225502_at	dedicator of cytokinesis 8	DOCK8	81704	4
204823_at	neuron navigator 3	NAV3	89795	4
212671_s_at	major histocompatibility complex, class II, DQ alpha 1	HLA-DQA1	3117	4
239233_at	KIAA1212	KIAA1212	55704	4
227817_at	Protein kinase C, beta 1	PRKCB1	5579	4
208010_s_at	protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	PTPN22	26191	4
242517_at	G protein-coupled receptor 54	GPR54	84634	4
1557718_at	protein phosphatase 2, regulatory subunit B (B56), gamma isoform	PPP2R5C	5527	4

Appendix D: Genes upregulated in AAA vs. NA (continued)

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
1553237_x_at	protocadherin alpha subfamily C, 1	PCDHAC1	56135	4
230245_s_at	hypothetical protein LOC283663	LOC283663	283663	4
230014_at	Yippee-like 5 (Drosophila)	YPEL5	51646	4
204363_at	coagulation factor III (thromboplastin, tissue factor)	F3	2152	4
225282_at	stromal membrane-associated protein 1-like	SMAP1L	64744	4
227346_at	Zinc finger protein, subfamily 1A, 1 (Ikaros)	ZNFN1A1	10320	4
219290_x_at	dual adaptor of phosphotyrosine and 3-phosphoinositides	DAPP1	27071	4
213888_s_at	TRAF3 interacting protein 3	TRAF3IP3	80342	4
205214_at	serine/threonine kinase 17b (apoptosis-inducing)	STK17B	9262	4
1562528_at	RAR-related orphan receptor A	RORA	6095	4
225706_at	glucocorticoid induced transcript 1	GLCCI1	113263	4
238581_at	Guanylate binding protein 5	GBP5	115362	4
234260_at	CDC42 small effector 2	CDC42SE2	56990	4
222326_at	Phosphodiesterase 4B, cAMP-specific (phosphodiesterase E4 dunce homolog, Drosophila)	PDE4B	5142	4
222858_s_at	dual adaptor of phosphotyrosine and 3-phosphoinositides	DAPP1	27071	4
201340_s_at	ectodermal-neural cortex (with BTB-like domain)	ENC1	8507	4
218723_s_at	response gene to complement 32	RGC32	28984	4
237104_at	Cathepsin S	CTSS	1520	4
222378_at	Hypothetical protein FLJ43663	FLJ43663	378805	4
212998_x_at	major histocompatibility complex, class II, DQ beta 1	HLA-DQB1	3119	4
200670_at	X-box binding protein 1	XBP1	7494	3
203178_at	glycine amidinotransferase (L-arginine:glycine amidinotransferase)	GATM	2628	3
1557459_at	SNF1-like kinase 2	SNF1LK2	23235	3
238063_at	hypothetical protein FLJ32028	FLJ32028	201799	3
211734_s_at	Fc fragment of IgE, high affinity I, receptor for; alpha polypeptide	FCER1A	2205	3

Appendix D: Genes upregulated in AAA vs. NA (continued)

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
204890_s_at	lymphocyte-specific protein tyrosine kinase	LCK	3932	3
217452_s_at	UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2	B3GALT2	8707	3
232213_at	Pellino homolog 1 (Drosophila)	PELI1	57162	3
205269_at	lymphocyte cytosolic protein 2 (SH2 domain containing leukocyte protein of 76kDa)	LCP2	3937	3
227266_s_at	FYN binding protein (FYB-120/130)	FYB	2533	3
227228_s_at	KIAA1509	KIAA1509	440193	3
204702_s_at	nuclear factor (erythroid-derived 2)-like 3	NFE2L3	9603	3
244023_at	Spleen tyrosine kinase	SYK	6850	3
213537_at	major histocompatibility complex, class II, DP alpha 1	HLA-DPA1	3113	3
233690_at	Chromosome 21 open reading frame 96	C21orf96	80215	3
204949_at	intercellular adhesion molecule 3	ICAM3	3385	3
241849_at	CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)	CD74	972	3
235086_at	Thrombospondin 1	THBS1	7057	3
206206_at	CD180 antigen	CD180	4064	3
210031_at	CD3Z antigen, zeta polypeptide (TiT3 complex)	CD3Z	919	3
240232_at	Chromosome 3 open reading frame 1	C3orf1	51300	3
205101_at	class II, major histocompatibility complex, transactivator	CIITA	4261	3
213416_at	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	ITGA4	3676	3
244172_at	B-cell linker	BLNK	29760	3
226930_at	fibronectin type III domain containing 1	FNDC1	84624	3
201688_s_at	tumor protein D52	TPD52	7163	3
220356_at	corin, serine peptidase	CORIN	10699	3
204057_at	interferon regulatory factor 8 ; interferon regulatory factor 8	IRF8	3394	3
206295_at	interleukin 18 (interferon-gamma-inducing factor)	IL18	3606	3
213765_at	microfibrillar associated protein 5	MFAP5	8076	3

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
212613_at	butyrophilin, subfamily 3, member A2	BTN3A2	11118	3
1555275_a_at	kelch-like 6 (Drosophila)	KLHL6	89857	3
1564164_at	hypothetical protein FLJ20054	FLJ20054	54530	3
219259_at	sema domain, immunoglobulin domain (Ig)	SEMA4A	64218	3
230970_at	Slingshot homolog 2 (Drosophila)	SSH2	85464	3
204613_at	phospholipase C, gamma 2 (phosphatidylinositol-specific)	PLCG2	5336	3
229014_at	hypothetical gene supported by AK124699	FLJ42709	441094	3
204204_at	solute carrier family 31 (copper transporters), member 2	SLC31A2	1318	3
201689_s_at	tumor protein D52	TPD52	7163	3
209030_s_at	immunoglobulin superfamily, member 4	IGSF4	23705	3
209758_s_at	microfibrillar associated protein 5	MFAP5	8076	3
209685_s_at	protein kinase C, beta 1	PRKCB1	5579	3
220988_s_at	C1q and tumor necrosis factor related protein 3	C1QTNF3	114899	3
1552584_at	interleukin 12 receptor, beta 1	IL12RB1	3594	3
209627_s_at	oxysterol binding protein-like 3	OSBPL3	26031	3
244599_at	Ceramide kinase-like	CERKL	375298	3
213975_s_at	leukocyte immunoglobulin-like receptor, subfamily B (with TM and ITIM domains), member 1	LILRB1	4069	3
1554050_at	sphingomyelin phosphodiesterase, acid-like 3B	SMPDL3B	27293	3
223620_at	G protein-coupled receptor 34	GPR34	2857	3
232181_at	hypothetical protein LOC153346	LOC153346	153346	3
1565544_at	ring finger protein 141	RNF141	50862	3
244251_at	Lymphocyte cytosolic protein 2 (SH2 domain containing leukocyte protein of 76kDa)	LCP2	3937	3
205456_at	CD3E antigen, epsilon polypeptide (TiT3 complex)	CD3E	916	3
201008_s_at	thioredoxin interacting protein	TXNIP	10628	3
1552703_s_at	caspase 1, apoptosis-related cysteine peptidase (interleukin 1, beta, convertase)	CASP1	114769	3

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
222245_s_at	fer-1-like 4 (C. elegans)	FER1L4	80307	3
240231_at	Antizyme inhibitor 1	OAZIN	51582	3
201739_at	serum/glucocorticoid regulated kinase	SGK	6446	3
233500_x_at	C-type lectin domain family 2, member D	CLEC2D	29121	3
203717_at	dipeptidylpeptidase 4 (CD26, adenosine deaminase complexing protein 2)	DPP4	1803	3
210340_s_at	colony stimulating factor 2 receptor, alpha, low-affinity (granulocyte-macrophage)	CSF2RA	1438	3
215894_at	prostaglandin D2 receptor (DP)	PTGDR	5729	3
242642_at	NudE nuclear distribution gene E homolog like 1 (A. nidulans)	NDEL1	81565	3
242482_at	protein kinase, cAMP-dependent, regulatory, type I, alpha (tissue specific extinguisher 1)	PRKAR1A	5573	3
205255_x_at	transcription factor 7 (T-cell specific, HMG-box)	TCF7	6932	3
205884_at	integrin, alpha 4 (antigen CD49D, alpha 4 subunit of VLA-4 receptor)	ITGA4	3676	3
206707_x_at	chromosome 6 open reading frame 32	C6orf32	9750	3
235735_at	Tumor necrosis factor (ligand) superfamily, member 8	TNFSF8	944	3
204044_at	quinolinate phosphoribosyltransferase (nicotinate-nucleotide pyrophosphorylase (carboxylating))	QPRT	23475	3
226560_at	Sphingosine-1-phosphate phosphotase 2	SGPP2	130367	3
244773_at	ATPase, aminophospholipid transporter (APLT), Class I, type 8A, member 1	ATP8A1	10396	3
214157_at	GNAS complex locus	GNAS	2778	3
1552953_a_at	neurogenic differentiation 2	NEUROD2	4761	3
204529_s_at	thymus high mobility group box protein TOX	TOX	9760	3
231794_at	cytotoxic T-lymphocyte-associated protein 4	CTLA4	1493	3
1558143_a_at	BCL2-like 11 (apoptosis facilitator)	BCL2L11	10018	3
215796_at	T cell receptor alpha variable 20	TRAV20	28663	3
206805_at	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3A	SEMA3A	10371	3
235522_at	C-type lectin domain family 2, member D	OCIL	29121	3

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
212951_at	G protein-coupled receptor 116	GPR116	221395	3
207075_at	cold autoinflammatory syndrome 1	CIAS1	114548	3
243819_at	Guanine nucleotide binding protein (G protein), gamma 2	GNG2	54331	3
1554455_at	lines homolog 1 (Drosophila)	LINS1	55180	3
209301_at	carbonic anhydrase II	CA2	760	3
201656_at	integrin, alpha 6	ITGA6	3655	3
242814_at	serpin peptidase inhibitor, clade B (ovalbumin), member 9	SERPINB9	5272	3
206176_at	bone morphogenetic protein 6	BMP6	654	3
1556698_a_at	hypothetical protein LOC285513	LOC285513	285513	3
1552658_a_at	neuron navigator 3	NAV3	89795	3
1555691_a_at	killer cell lectin-like receptor subfamily C, member 4	KLRC4	22914	3
226525_at	Serine/threonine kinase 17b (apoptosis-inducing)	STK17B	9262	3
233109_at	Collagen, type XII, alpha 1	COL12A1	1303	3
223862_at	ghrelin precursor	GHRL	51738	3
242268_at	CUG triplet repeat, RNA binding protein 2	CUGBP2	10659	3
235801_at	Tumor suppressor candidate 3	TUSC3	7991	3
236199_at	Arachidonate 5-lipoxygenase	ALOX5	240	3
230110_at	mucolipin 2	MCOLN2	255231	3
239901_at	Hypothetical protein FLJ43663	FLJ43663	378805	3
204197_s_at	runt-related transcription factor 3	RUNX3	864	3
205821_at	killer cell lectin-like receptor subfamily K, member 1	KLRK1	22914	3
208130_s_at	thromboxane A synthase 1 (platelet, cytochrome P450, family 5, subfamily A)	TBXAS1	6916	3
41577_at	protein phosphatase 1, regulatory (inhibitor) subunit 16B	PPP1R16B	26051	3
1559425_at	Protein kinase C, eta	PRKCH	5583	3

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
239835_at	kelch repeat and BTB (POZ) domain containing 8	KBTBD8	84541	3
206674_at	fms-related tyrosine kinase 3	FLT3	2322	3
235385_at	Membrane-associated ring finger (C3HC4) 1	MARCH-I	55016	3
236782_at	sterile alpha motif domain containing 3	SAMD3	154075	3
232635_at	chromosome 14 open reading frame 145	C14orf145	145508	3
238488_at	synleurin	SLRN	353281	3
241435_at	V-ets erythroblastosis virus E26 oncogene homolog 1 (avian)	ETS1	2113	3
212316_at	nucleoporin 210kDa	NUP210	23225	3
217192_s_at	PR domain containing 1, with ZNF domain	PRDM1	639	3
211654_x_at	major histocompatibility complex, class II, DQ beta 1	HLA-DQB1	3119	3
203854_at	I factor (complement)	IF	3426	3
215392_at	Ubiquitin specific peptidase 3	USP3	9960	3
209823_x_at	major histocompatibility complex, class II, DQ beta 1	HLA-DQB1	3119	3
217394_at	T cell receptor alpha locus	TRA@	6955	3
206637_at	purinergic receptor P2Y, G-protein coupled, 14	P2RY14	9934	3
228055_at	napsin B aspartic peptidase pseudogene	NAPSB	256236	3
236921_at	Embigin homolog (mouse)	EMB	133418	3
205467_at	caspase 10, apoptosis-related cysteine peptidase	CASP10	843	3
210040_at	solute carrier family 12, (potassium-chloride transporter) member 5	SLC12A5	57468	3
1560486_at	syntaxin binding protein 3	STXBP3	6814	3
204995_at	cyclin-dependent kinase 5, regulatory subunit 1 (p35)	CDK5R1	8851	3
226878_at	major histocompatibility complex, class II, DO alpha	HLA-DOA	3111	3
206370_at	phosphoinositide-3-kinase, catalytic, gamma polypeptide	PIK3CG	5294	3
215930_s_at	CTAGE family, member 5	CTAGE5	4253	3

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
1560754_at	chemokine-like factor superfamily 7	CKLFSF7	112616	3
204623_at	trefoil factor 3 (intestinal)	TFF3	7033	3
236422_at	Hypothetical protein FLJ22662	FLJ22662	79887	3
239260_at	corin, serine peptidase	CORIN	10699	3
242210_at	Zinc finger protein 24 (KOX 17)	ZNF24	7572	3
205504_at	Bruton agammaglobulinemia tyrosine kinase	BTK	695	3
221698_s_at	C-type lectin domain family 7, member A ; C-type lectin domain family 7, member A	CLEC7A	64581	3
210184_at	integrin, alpha X (antigen CD11C (p150), alpha polypeptide)	ITGAX	3687	3
238452_at	Fc receptor-like and mucin-like 2	FCRLM2	127943	3
203416_at	CD53 antigen	CD53	963	3
217478_s_at	major histocompatibility complex, class II, DM alpha	HLA-DMA	3108	3
227344_at	Zinc finger protein, subfamily 1A, 1 (Ikaros)	ZNFN1A1	10320	3
220560_at	chromosome 11 open reading frame 21	C11orf21	29125	3
209846_s_at	butyrophilin, subfamily 3, member A2	BTN3A2	11118	3
212950_at	G protein-coupled receptor 116	GPR116	221395	3
229383_at	Membrane-associated ring finger (C3HC4) 1	MARCH-I	55016	3
206608_s_at	retinitis pigmentosa GTPase regulator interacting protein 1	RPGRIP1	57096	3
209696_at	fructose-1,6-bisphosphatase 1	FBP1	2203	3
229802_at	WNT1 inducible signaling pathway protein 1	WISP1	8840	3
208763_s_at	TSC22 domain family, member 3	TSC22D3	1831	3
230550_at	membrane-spanning 4-domains, subfamily A, member 6A	MS4A6A	64231	3
227014_at	similar to aspartate beta hydroxylase (ASPH)	LOC57168	57168	3
1558783_at	Wilms tumor 1 associated protein	WTAP	9589	3
213915_at	natural killer cell group 7 sequence	NKG7	4818	3
209626_s_at	oxysterol binding protein-like 3	OSBPL3	26031	3

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
38521_at	myelin associated glycoprotein	MAG	4099	3
210038_at	protein kinase C, theta	PRKCQ	5588	3
228113_at	RAB37, member RAS oncogene family	RAB37	326624	3
202524_s_at	sparc/osteonectin, cwcv and kazal-like domains proteoglycan (testican) 2	SPOCK2	9806	3
223358_s_at	Phosphodiesterase 7A	PDE7A	5150	3
205987_at	CD1C antigen, c polypeptide	CD1C	911	3
239893_at	Multiple C2-domains with two transmembrane regions 2	MCTP2	55784	3
AFFX-M27830	SRY (sex determining region Y)-box 18	SOX18	54345	3
1554786_at	chromosome 20 open reading frame 32	C20orf32	57091	3
213036_x_at	ATPase, Ca++ transporting, ubiquitous	ATP2A3	489	3
212543_at	absent in melanoma 1	AIM1	202	3
232687_at	Hypothetical protein LOC285513	LOC285513	285513	3
215243_s_at	gap junction protein, beta 3, 31kDa (connexin 31)	GJB3	2707	3
226150_at	Phosphatidic acid phosphatase type 2 domain containing 1B	HTPAP	84513	3
238790_at	CLR pseudogene	LOC374443	374443	3
204852_s_at	protein tyrosine phosphatase, non-receptor type 7	PTPN7	5778	3
206278_at	platelet-activating factor receptor	PTAFR	5724	3
215483_at	A kinase (PRKA) anchor protein (yotiao) 9	AKAP9	10142	3
1554545_at	chromosome 1 open reading frame 169	C1orf169	403314	3
239162_at	Death-associated protein kinase 1	DAPK1	1612	3
205698_s_at	mitogen-activated protein kinase kinase 6	MAP2K6	5608	3
225700_at	glucocorticoid induced transcript 1	GLCCI1	113263	3
202295_s_at	cathepsin H	CTSH	1512	3

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
243403_x_at	carboxypeptidase M	CPM	1368	3
219313_at	hypothetical protein DKFZp434C0328	DKF	54762	3
220646_s_at	killer cell lectin-like receptor subfamily F, member 1	KLRF1	51348	3
243465_at	Hypothetical protein FLJ11000	FLJ11000	55281	3
219690_at	U2(RNU2) small nuclear RNA auxiliary factor 1-like 4	U2AF1L4	79713	3
243993_at	PCTAIRE protein kinase 2	PCTK2	5128	3
205297_s_at	CD79B antigen (immunoglobulin-associated beta)	CD79B	974	3
207794_at	chemokine (C-C motif) receptor 2 ; chemokine (C-C motif) receptor 2	CCR2	1231	3
1568830_at	RNA binding motif, single stranded interacting protein 1	IRAK3	11213	3
228869_at	Selectin ligand interactor cytoplasmic-1	SLIC1	124460	3
1558120_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 3, X-linked	DDX3X	1654	3
241765_at	carboxypeptidase M	CPM	1368	3
229958_at	chromosome 8 open reading frame 61	C8orf61	619435	3
239586_at	family with sequence similarity 83, member A	FAM83A	84985	3
225606_at	BCL2-like 11 (apoptosis facilitator)	BCL2L11	10018	3
234996_at	Calcitonin receptor-like	CALCRL	10203	3
232304_at	Pellino homolog 1 (Drosophila)	PELI1	57162	3
217302_at	olfactory receptor, family 2, subfamily F, member 2	OR2F2	135948	3
204959_at	myeloid cell nuclear differentiation antigen ; myeloid cell nuclear differentiation antigen	MNDA	4332	3
1559654_s_at	Growth hormone regulated TBC protein 1	GRTP1	79774	3
212699_at	secretory carrier membrane protein 5	SCAMP5	192683	3
212732_at	maternally expressed 3	MEG3	55384	3
233867_at	Zinc finger, SWIM-type containing 6	MGC40405	257415	3
1557558_s_at	Matrilin 1, cartilage matrix protein	MATN1	4146	3

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
1564077_at	Hypothetical protein LOC285513	LOC285513	285513	3
223851_s_at	tumor necrosis factor receptor superfamily, member 18	TNFRSF18	8784	3
226517_at	branched chain aminotransferase 1, cytosolic	BCAT1	586	3
207735_at	ring finger protein 125	RNF125	54941	3
207957_s_at	Protein kinase C, beta 1	PRKCB1	5579	3
206118_at	signal transducer and activator of transcription 4	STAT4	6775	3
201690_s_at	tumor protein D52	TPD52	7163	3
210039_s_at	protein kinase C, theta	PRKCQ	5588	3
226659_at	differentially expressed in FDCP 6 homolog (mouse)	DEF6	50619	3
223218_s_at	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta	NFKBIZ	64332	3
243765_at	SEC31-like 1 (S. cerevisiae)	SEC31L1	22872	3
1554519_at	CD80 antigen (CD28 antigen ligand 1, B7-1 antigen)	CD80	941	3
204265_s_at	G-protein signalling modulator 3 (AGS3-like, C. elegans)	GPSM3	63940	3
228071_at	GTPase, IMAP family member 7	GIMAP7	168537	3
231310_at	Transcribed locus			3
226991_at	Nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2	NFATC2	4773	3
235970_at	transcription factor MLR1	MLR1	254251	3
204820_s_at	butyrophilin, subfamily 3, member A3	BTN3A3	10384	3
237461_at	NACHT, leucine rich repeat and PYD containing 7	NALP7	199713	3
234167_at	Hypothetical protein LOC254128	MKI67IP	84365	3
1559848_at	NOL1/NOP2/Sun domain family, member 4	NSUN4	387338	3
201009_s_at	thioredoxin interacting protein	TXNIP	10628	3
238593_at	hypothetical protein FLJ22531	FLJ22531	79703	3
243764_at	V-set and immunoglobulin domain containing 1	VSIG1	340547	3

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
209032_s_at	immunoglobulin superfamily, member 4	IGSF4	23705	3
235706_at	carboxypeptidase M	CPM	1368	3
224046_s_at	phosphodiesterase 7A	PDE7A	5150	3
240260_at	Protein tyrosine phosphatase, non-receptor type 1	PTPN1	5770	3
219947_at	C-type lectin domain family 4, member A	CLEC4A	50856	3
1562529_s_at	RAR-related orphan receptor A	RORA	6095	3
207426_s_at	tumor necrosis factor (ligand) superfamily, member 4	TNFSF4	7292	3
235574_at	guanylate binding protein 4	GBP4	115361	3
214181_x_at	leukocyte specific transcript 1	LST1	7940	3
236528_at	Ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast)	UBE2J1	51465	2
238062_at	high density lipoprotein-binding protein	LOC338328	338328	2
239957_at	Hypothetical protein FLJ10707	FLJ10707	55209	2
1569369_at	Zinc finger, FYVE domain containing 28	ZFYVE28	57732	2
233252_s_at	spermatid perinuclear RNA binding protein	STRBP	55342	2
205801_s_at	RAS guanyl releasing protein 3 (calcium and DAG-regulated)	RASGRP3	25780	2
209496_at	retinoic acid receptor responder (tazarotene induced) 2	RARRES2	5919	2
208109_s_at	chromosome 15 open reading frame 5 ; chromosome 15 open reading frame 5	C15orf5	81698	2
202450_s_at	cathepsin K (pycnodysostosis)	CTSK	1513	2
228754_at	solute carrier family 6 (neurotransmitter transporter, taurine), member 6	SLC6A6	6533	2
229513_at	Spermatid perinuclear RNA binding protein	STRBP	55342	2
204897_at	prostaglandin E receptor 4 (subtype EP4)	PTGER4	5734	2
244033_at	chromosome 14 open reading frame 145	C14orf145	145508	2
229070_at	chromosome 6 open reading frame 105	C6orf105	84830	2
38149_at	Rho GTPase activating protein 25	ARHGAP25	9938	2

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
204101_at	myotubularin 1	MTM1	4534	2
201236_s_at	BTG family, member 2	BTG2	7832	2
205027_s_at	mitogen-activated protein kinase kinase kinase 8	MAP3K8	1326	2
243395_at	Decay accelerating factor for complement (CD55, Cromer blood group system)	DAF	1604	2
1553096_s_at	BCL2-like 11 (apoptosis facilitator)	BCL2L11	10018	2
1553271_at	KIAA1463 protein	KIAA1463	57609	2
39402_at	interleukin 1, beta	IL1B	3553	2
223217_s_at	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, zeta	NFKBIZ	64332	2
228793_at	jumonji domain containing 1C	JMJD1C	221037	2
217984_at	ribonuclease T2	RNASET2	8635	2
235380_at	Arachidonate 5-lipoxygenase	ALOX5	240	2
1552634_a_at	zinc finger protein 101	ZNF101	94039	2
243066_at	N-acetylneuraminate pyruvate lyase (dihydrodipicolinate synthase)	NPL	80896	2
205651_x_at	Rap guanine nucleotide exchange factor (GEF) 4	RAPGEF4	11069	2
205920_at	solute carrier family 6 (neurotransmitter transporter, taurine), member 6	SLC6A6	6533	2
232835_at	Jumonji, AT rich interactive domain 2	JARID2	3720	2
214518_at	pyruvate dehydrogenase (lipoamide) alpha 2	PDHA2	5161	2
226677_at	zinc finger protein 521	ZNF521	25925	2
201669_s_at	myristoylated alanine-rich protein kinase C substrate	MARCKS	4082	2
207686_s_at	caspase 8, apoptosis-related cysteine peptidase	CASP8	841	2
232455_x_at	hypothetical protein LOC340085	LOC340085	340085	2
1554202_x_at	calcium binding protein 4	CABP4	57010	2
206765_at	potassium inwardly-rectifying channel, subfamily J, member 2	KCNJ2	3759	2

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
218035_s_at	RNA-binding protein	FLJ20273	54502	2
222307_at	hypothetical protein LOC282997	LOC282997	282997	2
219700_at	plexin domain containing 1	PLXDC1	57125	2
205789_at	CD1D antigen, d polypeptide ; CD1D antigen, d polypeptide	CD1D	912	2
205988_at	CD84 antigen (leukocyte antigen)	CD84	8832	2
244388_at	Wingless-type MMTV integration site family, member 5A	WNT5A	7474	2
221648_s_at	chromosome 1 open reading frame 121	C1orf121	51029	2
215633_x_at	leukocyte specific transcript 1	LST1	7940	2
215775_at	Thrombospondin 1	THBS1	7057	2
230590_at	Slingshot homolog 2 (Drosophila)	SSH2	85464	2
1557145_at	Serine/threonine kinase 38	STK38	11329	2
226020_s_at	disabled homolog 1 (Drosophila) ; OMA1 homolog, zinc metallopeptidase (S. cerevisiae)	DAB1 ; OMA1	115209 ; 1600	2
221080_s_at	DENN/MADD domain containing 1C	DENND1C	79958	2
238332_at	ankyrin repeat domain 29	ANKRD29	147463	2
227354_at	phosphoprotein associated with glycosphingolipid microdomains 1	PAG1	55824	2
1552519_at	activin A receptor, type IC	ACVR1C	130399	2
213506_at	coagulation factor II (thrombin) receptor-like 1	F2RL1	2150	2
233011_at	Annexin A1	ANXA1	301	2
222062_at	interleukin 27 receptor, alpha	IL27RA	9466	2
206896_s_at	guanine nucleotide binding protein (G protein), gamma 7	GNG7	2788	2
1559249_at	Ataxin 1	ATXN1	6310	2
237051_at	Solute carrier family 30 (zinc transporter), member 9	SLC30A9	10463	2
219694_at	hypothetical protein FLJ11127	FLJ11127	54491	2
226039_at	Mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isoenzyme A	MGAT4A	11320	2

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
237001_at	NIK and IKK binding protein	T1	83696	2
1561390_at	family with sequence similarity 41, member A, Y-linked	FAM41AY	340618	2
203028_s_at	cytochrome b-245, alpha polypeptide	CYBA	1535	2
205898_at	chemokine (C-X3-C motif) receptor 1	CX3CR1	1524	2
213475_s_at	integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	ITGAL	3683	2
242672_at	Raft-linking protein	RAFTLIN	23180	2
205038_at	Zinc finger protein, subfamily 1A, 1 (Ikaros)	ZNFN1A1	10320	2
209281_s_at	ATPase, Ca++ transporting, plasma membrane 1	ATP2B1	490	2
219602_s_at	family with sequence similarity 38, member B	FAM38B	63895	2
224797_at	arrestin domain containing 3	ARRDC3	57561	2
214574_x_at	leukocyte specific transcript 1	LST1	7940	2
232793_at	Immunoglobulin superfamily, member 4	IGSF4	23705	2
1552541_at	T-cell activation GTPase activating protein	TAGAP	117289	2
44790_s_at	chromosome 13 open reading frame 18	C13orf18	80183	2
205288_at	CDC14 cell division cycle 14 homolog A (S. cerevisiae)	CDC14A	8556	2
219501_at	hypothetical protein FLJ10094	FLJ10094	55068	2
214148_at	Forkhead box M1	FOXM1	2305	2
238439_at	ankyrin repeat domain 22	ANKRD22	118932	2
218322_s_at	acyl-CoA synthetase long-chain family member 5	ACSL5	51703	2
239938_x_at	MADS box transcription enhancer factor 2, polypeptide C (myocyte enhancer factor 2C)	MEF2C	4208	2
208056_s_at	core-binding factor, runt domain, alpha subunit 2; translocated to, 3	CBFA2T3	863	2
206316_s_at	kinetochore associated 1	KNTC1	9735	2
1554462_a_at	DnaJ (Hsp40) homolog, subfamily B, member 9	DNAJB9	4189	2

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
221586_s_at	E2F transcription factor 5, p130-binding	E2F5	1875	2
205471_s_at	dachshund homolog 1 (Drosophila)	DACH1	1602	2
218746_at	TAP binding protein-like	TAPBPL	55080	2
205685_at	CD86 antigen (CD28 antigen ligand 2, B7-2 antigen)	CD86	942	2
241027_at	optic atrophy 1 (autosomal dominant)	OPA1	4976	2
223322_at	Ras association (RalGDS/AF-6) domain family 5	RASSF5	83593	2
217168_s_at	homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	HERPUD1	9709	2
217120_s_at	cofactor required for Sp1 transcriptional activation, subunit 2, 150kDa	CRSP2	9282	2
203317_at	pleckstrin and Sec7 domain containing 4	PSD4	23550	2
210176_at	toll-like receptor 1	TLR1	7096	2
213373_s_at	caspase 8, apoptosis-related cysteine peptidase	CASP8	841	2
236067_at	Muscleblind-like 2 (Drosophila)	MBNL2	10150	2
234562_x_at	Chemokine-like factor superfamily 8	CKLFSF8	152189	2
211286_x_at	colony stimulating factor 2 receptor, alpha, low-affinity (granulocyte-macrophage)	CSF2RA	1438	2
232565_at	RAB6 interacting protein 2	RAB6IP2	23085	2
208981_at	platelet/endothelial cell adhesion molecule (CD31 antigen)	PECAM1	5175	2
236345_at	Thromboxane A synthase 1 (platelet, cytochrome P450, family 5, subfamily A)	TBXAS1	6916	2
207038_at	solute carrier family 16 (monocarboxylic acid transporters), member 6	SLC16A6	9120	2
232034_at	hypothetical protein LOC203274	LOC203274	203274	2
241843_at	Eukaryotic translation initiation factor 5	EIF5	1983	2
229750_at	POU domain, class 2, transcription factor 2	POU2F2	5452	2
220684_at	T-box 21	TBX21	30009	2
213317_at	Chloride intracellular channel 5	CLIC5	53405	2

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
1565598_at	RNA-binding protein	FLJ20273	54502	2
205551_at	synaptic vesicle glycoprotein 2B	SV2B	9899	2
201324_at	epithelial membrane protein 1	EMP1	2012	2
232744_x_at	Ataxin 1	ATXN1	6310	2
211582_x_at	leukocyte specific transcript 1	LST1	7940	2
205554_s_at	deoxyribonuclease I-like 3	DNASE1L3	1776	2
207890_s_at	matrix metallopeptidase 25	MMP25	64386	2
239336_at	Thrombospondin 1	THBS1	7057	2
239167_at	AF4/FMR2 family, member 1	MLLT2	4299	2
227558_at	chromobox homolog 4 (Pc class homolog, Drosophila)	CBX4	8535	2
213017_at	abhydrolase domain containing 3	ABHD3	171586	2
239122_at	Interleukin 24	IL24	11009	2
205945_at	interleukin 6 receptor ; interleukin 6 receptor	IL6R	3570	2
1560625_s_at	Hypothetical gene supported by BC052750	MGC50811	375307	2
1564333_a_at	Sortilin-related VPS10 domain containing receptor 2	SORCS2	57537	2
207522_s_at	ATPase, Ca++ transporting, ubiquitous	ATP2A3	489	2
209993_at	ATP-binding cassette, sub-family B (MDR/TAP), member 1	ABCB1	5243	2
236808_at	FGFR1 oncogene partner 2	FGFR1OP2	26127	2
227867_at	hypothetical protein LOC129293	LOC129293	129293	2
213496_at	plasticity related gene 1	LPPR4	9890	2
228442_at	Nuclear factor of activated T-cells, cytoplasmic, calcineurin-dependent 2	NFATC2	4773	2
1556001_at	hypothetical protein LOC284939	LOC284939	284939	2
220603_s_at	multiple C2-domains with two transmembrane regions 2	MCTP2	55784	2
244341_at	Mak3 homolog (S. cerevisiae)	MAK3	80218	2

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
223717_s_at	acrosin binding protein	ACRBP	84519	2
215051_x_at	allograft inflammatory factor 1	AIF1	199	2
201110_s_at	thrombospondin 1	THBS1	7057	2
217983_s_at	ribonuclease T2	RNASET2	8635	2
230792_at	hypothetical protein FLJ31204	FLJ31204	158584	2
230789_at	suppressor of hairy wing homolog 2 (Drosophila)	SUHW2	140883	2
242558_at	Catenin (cadherin-associated protein), beta 1, 88kDa	CTNNB1	1499	2
241837_at	AT rich interactive domain 5B (MRF1-like)	ARID5B	84159	2
201149_s_at	TIMP metallopeptidase inhibitor 3 (Sorsby fundus dystrophy, pseudoinflammatory)	TIMP3	7078	2
1556643_at	Hypothetical protein BC011840	LOC93343	93343	2
223709_s_at	wingless-type MMTV integration site family, member 10A	WNT10A	80326	2
223922_x_at	membrane-spanning 4-domains, subfamily A, member 6A	MS4A6A	64231	2
244650_at	Hypothetical protein FLJ11127	FLJ11127	54491	2
1559413_at	T-complex 11 (mouse) like 2	MGC40368	255394	2
234900_at	similar to dJ612B18.1 (similar to 40S ribosomal protein)	LOC391137	391137	2
239096_at	Chromosome 14 open reading frame 32	C14orf32	93487	2
238886_at	Transmembrane emp24-like trafficking protein 10 (yeast)	TMP21	10972	2
205865_at	AT rich interactive domain 3A (BRIGHT- like)	ARID3A	1820	2
224480_s_at	hypothetical protein MGC11324 ; hypothetical protein MGC11324	MGC11324	84803	2
238428_at	potassium inwardly-rectifying channel, subfamily J, member 15	KCNJ15	3772	2
1569600_at	BCMS upstream neighbor-like	BCMSUNL	79469	2
209770_at	butyrophilin, subfamily 3, member A1	BTN3A1	11119	2
208982_at	Platelet/endothelial cell adhesion molecule (CD31 antigen)	PECAM1	5175	2
240094_at	Thioredoxin domain containing 13	DJ971N18.2	56255	2

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
207414_s_at	proprotein convertase subtilisin/kexin type 6	PCSK6	5046	2
236436_at	hypothetical protein LOC283130	LOC283130	283130	2
226333_at	interleukin 6 receptor	IL6R	3570	2
201108_s_at	thrombospondin 1	THBS1	7057	2
228575_at	fibronectin type III domain containing 6	FNDC6	152028	2
218751_s_at	F-box and WD-40 domain protein 7 (archipelago homolog, Drosophila)	FBXW7	55294	2
243362_s_at	lymphoid enhancer-binding factor 1	LEF1	51176	2
208119_s_at	zinc finger protein 505 ; zinc finger protein 505	ZNF505	81931	2
210538_s_at	baculoviral IAP repeat-containing 3	BIRC3	330	2
204061_at	protein kinase, X-linked	PRKX	5613	2
214590_s_at	ubiquitin-conjugating enzyme E2D 1 (UBC4/5 homolog, yeast)	UBE2D1	7321	2
242239_at	NOL1/NOP2/Sun domain family, member 6	NSUN6	221078	2
214772_at	chromosome 11 open reading frame 41	C11orf41	25758	2
244377_at	Solute carrier family 1 (glutamate/neutral amino acid transporter), member 4	SLC1A4	6509	2
238812_at	Zinc finger, A20 domain containing 3	ZA20D3	54469	2
239579_at	abhydrolase domain containing 7	ABHD7	253152	2
236313_at	cyclin-dependent kinase inhibitor 2B (p15, inhibits CDK4)	CDKN2B	1030	2
210982_s_at	major histocompatibility complex, class II, DR alpha	HLA-DRA	3122	2
230438_at	T-box 15	TBX15	6913	2
226474_at	nucleotide-binding oligomerization domains 27	NOD27	84166	2
229214_at	Syntaxin 7	STX7	8417	2
217825_s_at	ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast)	UBE2J1	51465	2
206036_s_at	v-rel reticuloendotheliosis viral oncogene homolog (avian)	REL	5966	2
229819_at	alpha-1-B glycoprotein	A1BG	1	2

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
59644_at	BMP2 inducible kinase	BMP2K	55589	2
238423_at	synaptotagmin-like 3	SYTL3	94120	2
201733_at	chloride channel 3	CLCN3	1182	2
209946_at	vascular endothelial growth factor C	VEGFC	7424	2
227761_at	myosin VA (heavy polypeptide 12, myoxin)	MYO5A	4644	2
1565754_x_at	FYVE, RhoGEF and PH domain containing 2	FGD2	221472	2
208368_s_at	breast cancer 2, early onset	BRCA2	675	2
219577_s_at	ATP-binding cassette, sub-family A (ABC1), member 7	ABCA7	10347	2
1556931_at	Cell division cycle 42 (GTP binding protein, 25kDa)	CDC42	998	2
201148_s_at	TIMP metallopeptidase inhibitor 3 (Sorsby fundus dystrophy, pseudoinflammatory)	TIMP3	7078	2
233816_at	Solute carrier family 8 (sodium/calcium exchanger), member 1	SLC8A1	6546	2
214735_at	phosphoinositide-binding protein PIP3-E	PIP3-E	26034	2
236285_at	Kelch domain containing 7B	MGC16635	113730	2
1563357_at	Serpin peptidase inhibitor, clade B (ovalbumin), member 9	SERPINB9	5272	2
232797_at	Integrin, alpha V (vitronectin receptor, alpha polypeptide, antigen CD51)	ITGAV	3685	2
1565913_at	Zinc finger CCCH-type, antiviral 1	ZC3HAV1	56829	2
206995_x_at	scavenger receptor class F, member 1	SCARF1	8578	2
213142_x_at	hypothetical protein LOC54103	LOC54103	54103	2
211129_x_at	ectodysplasin A	EDA	1896	2
204602_at	dickkopf homolog 1 (Xenopus laevis)	DKK1	22943	2
235780_at	protein kinase, cAMP-dependent, catalytic, beta	PRKACB	5567	2
206508_at	tumor necrosis factor (ligand) superfamily, member 7	TNFSF7	970	2
239489_at	Ubiquitin-like domain containing CTD phosphatase 1	MGC10067	134510	2
242384_at	Cytoplasmic polyadenylation element binding protein 4	CPEB4	80315	2

Appendix D: Genes upregulated in AAA vs. NA (continued).

Probe	Gene Description	Gene symbol	Entrez Gene ID	Fold change
1566446_at	Kruppel-like factor 12	KLF12	11278	2
235486_at	hypothetical protein MGC34830	MGC34830	120196	2
244020_at	Hypothetical protein MGC13204	MGC13204	83695	2
206377_at	forkhead box F2	FOXF2	2295	2
236395_at	MADS box transcription enhancer factor 2, polypeptide C (myocyte enhancer factor 2C)	MEF2C	4208	2
211799_x_at	major histocompatibility complex, class I, C	HLA-C	3107	2
227372_s_at	BAI1-associated protein 2-like 1	BAIAP2L1	55971	2
217715_x_at	Zinc finger protein 354A	ZNF354A	6940	2
227686_at	hypothetical protein BC008322	MGC15763	92106	2
230609_at	enthoprotin	ENTH	9685	2
201109_s_at	thrombospondin 1	THBS1	7057	2
214567_s_at	chemokine (C motif) ligand 1 ; chemokine (C motif) ligand 2	XCL1 ; XCL2	6375 ; 6846	2
203988_s_at	fucosyltransferase 8 (alpha (1,6) fucosyltransferase)	FUT8	2530	2
224388_s_at	collagen, type XXV, alpha 1 ; collagen, type XXV, alpha 1	COL25A1	84570	2
1554616_at	serpin peptidase inhibitor, clade B (ovalbumin), member 8	SERPINB8	5271	2
240363_at	ankyrin 1, erythrocytic	ANK1	286	2
201147_s_at	TIMP metallopeptidase inhibitor 3 (Sorsby fundus dystrophy, pseudoinflammatory)	TIMP3	7078	2
1552322_at	hypothetical protein BC017868	RP3-473B4.1	159091	2
205080_at	retinoic acid receptor, beta	RARB	5915	2
211842_s_at	solute carrier family 24 (sodium/potassium/calcium exchanger), member 1	SLC24A1	9187	2
229765_at	Transcribed locus			2

Appendix E: Genes downregulated in AAA vs. NA

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
205265_s_at	aortic preferentially expressed gene 1	APEG1	10290	56
232067_at	chromosome 6 open reading frame 168	C6orf168	84553	24
213479_at	neuronal pentraxin II	NPTX2	4885	16
203295_s_at	ATPase, Na+/K+ transporting, alpha 2 (+) polypeptide	ATP1A2	477	16
214586_at	G protein-coupled receptor 37 (endothelin receptor type B-like)	GPR37	2861	16
220677_s_at	ADAM metallopeptidase with thrombospondin type 1 motif, 8	ADAMTS8	11095	15
224219_s_at	transient receptor potential cation channel, subfamily C, member 4	TRPC4	7223	14
214978_s_at	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 4	PPFIA4	8497	14
231859_at	chromosome 14 open reading frame 132	C14orf132	56967	14
221215_s_at	receptor-interacting serine-threonine kinase 4	RIPK4	54101	13
205675_at	microsomal triglyceride transfer protein (large polypeptide, 88kDa)	MTP	4547	13
204100_at	thyroid hormone receptor, alpha (erythroblastic leukemia viral (v-erb-a) oncogene homolog, avian)	THRA	7067	12
228695_at	chromosome 8 open reading frame 46	C8orf46	254778	12
227441_s_at	E2a-Pbx1-associated protein	EB-1	56899	12
1557315_a_at	Astrotactin 2	ASTN2	23245	12
1557795_s_at	neurotrophic tyrosine kinase, receptor, type 3	NTRK3	4916	12
205413_at	metallophosphoesterase domain containing 2	MPPED2	744	12
207557_s_at	ryanodine receptor 2 (cardiac)	RYR2	6262	12
213745_at	attractin-like 1	ATRNL1	26033	11
228449_at	Hypothetical protein FLJ35801	FLJ35801	150291	11
206766_at	integrin, alpha 10	ITGA10	8515	11
215025_at	neurotrophic tyrosine kinase, receptor, type 3	NTRK3	4916	11
228796_at	copine IV	CPNE4	131034	11
207317_s_at	calsequestrin 2 (cardiac muscle)	CASQ2	845	10

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
206277_at	purinergic receptor P2Y, G-protein coupled, 2	P2RY2	5029	10
241412_at	betacellulin	BTC	685	10
227819_at	leucine-rich repeat-containing G protein-coupled receptor 6	LGR6	59352	10
224457_at	hypothetical protein MGC12982 ; hypothetical protein MGC12982	MGC12982	84793	9
224220_x_at	transient receptor potential cation channel, subfamily C, member 4	TRPC4	7223	9
1564736_a_at	caspase 12 pseudogene 1	CASP12P1	120329	9
1555725_a_at	regulator of G-protein signalling 5	RGS5	8490	9
226415_at	KIAA1576 protein	KIAA1576	57687	9
203296_s_at	ATPase, Na+/K+ transporting, alpha 2 (+) polypeptide	ATP1A2	477	9
203766_s_at	leiomodin 1 (smooth muscle)	LMOD1	25802	9
230463_at	Synapsin II	SYN2	6854	9
1554702_at	voltage gated channel like 1	VGCNL1	259232	9
205893_at	neuroligin 1	NLGN1	22871	9
204953_at	synaptosomal-associated protein, 91kDa homolog (mouse)	SNAP91	9892	9
233059_at	Potassium inwardly-rectifying channel, subfamily J, member 3	KCNJ3	3760	9
226523_at	Proprotein convertase subtilisin/kexin type 7	PCSK7	9159	9
206462_s_at	neurotrophic tyrosine kinase, receptor, type 3	NTRK3	4916	9
201496_x_at	myosin, heavy polypeptide 11, smooth muscle	MYH11	4629	9
219295_s_at	procollagen C-endopeptidase enhancer 2	PCOLCE2	26577	9
214966_at	glutamate receptor, ionotropic, kainate 5	GRIK5	2901	9
204284_at	protein phosphatase 1, regulatory (inhibitor) subunit 3C	PPP1R3C	5507	9
218864_at	tensin 1	TNS1	7145	9
201481_s_at	phosphorylase, glycogen; brain	PYGB	5834	8
221319_at	protocadherin beta 8	PCDHB8	56128	8

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
205475_at	scrapie responsive protein 1	SCRG1	11341	8
209441_at	Rho-related BTB domain containing 2	RHOBTB2	23221	8
225548_at	shroom	SHRM	57619	8
230311_s_at	PR domain containing 6	PRDM6	93166	8
221747_at	Tensin 1 ; Tensin 1	TNS	7145	8
219167_at	RAS-like, family 12	RASL12	51285	8
228716_at	thyroid hormone receptor, beta (erythroblastic leukemia viral (v-erb-a) oncogene homolog 2, avian)	THRB	7068	8
228849_at	neurotrophic tyrosine kinase, receptor, type 3	NTRK3	4916	8
214044_at	ryanodine receptor 2 (cardiac)	RYR2	6262	8
206389_s_at	phosphodiesterase 3A, cGMP-inhibited	PDE3A	5139	8
219743_at	hairy/enhancer-of-split related with YRPW motif 2	HEY2	23493	8
228182_at	adenylate cyclase 5	ADCY5	111	8
1555819_s_at	hypothetical protein LOC201191	LOC201191	201191	8
244058_at	chromosome 10 open reading frame 72	C10orf72	196740	8
234971_x_at	phospholipase C, delta 3	PLCD3	113026	7
226325_at	adenylosuccinate synthase like 1	ADSSL1	122622	7
209621_s_at	PDZ and LIM domain 3	PDLIM3	27295	7
233442_at	PDZ domain containing RING finger 3	PDZRN3	23024	7
222771_s_at	myelin expression factor 2	MYEF2	50804	7
1558828_s_at	hypothetical gene supported by BX640700	LOC401212	401212	7
209081_s_at	collagen, type XVIII, alpha 1	COL18A1	80781	7
207961_x_at	myosin, heavy polypeptide 11, smooth muscle	MYH11	4629	7
210869_s_at	melanoma cell adhesion molecule	MCAM	4162	7
217377_x_at	neurotrophic tyrosine kinase, receptor, type 3	NTRK3	4916	7
229657_at	thyroid hormone receptor, beta (erythroblastic leukemia viral (v-erb-a) oncogene homolog 2, avian)	THRB	7068	7

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
217033_x_at	neurotrophic tyrosine kinase, receptor, type 3	NTRK3	4916	7
227088_at	phosphodiesterase 5A, cGMP-specific	PDE5A	8654	7
230104_s_at	brain-specific protein p25 alpha	TPPP	11076	7
203756_at	Rho guanine nucleotide exchange factor (GEF) 17	ARHGEF17	9828	7
206757_at	phosphodiesterase 5A, cGMP-specific	PDE5A	8654	7
215115_x_at	neurotrophic tyrosine kinase, receptor, type 3	NTRK3	4916	7
223843_at	scavenger receptor class A, member 3	SCARA3	51435	7
204846_at	ceruloplasmin (ferroxidase)	CP	1356	7
221280_s_at	par-3 partitioning defective 3 homolog (C. elegans)	PARD3	56288	7
205957_at	plexin B3	PLXNB3	5365	7
240045_at	PR domain containing 16	PRDM16	63976	7
218087_s_at	sorbin and SH3 domain containing 1	SORBS1	10580	7
209087_x_at	melanoma cell adhesion molecule	MCAM	4162	6
227440_at	E2a-Pbx1-associated protein	EB-1	56899	6
211094_s_at	neurofibromin 1 (neurofibromatosis, von Recklinghausen disease, Watson disease)	NF1	4763	6
203951_at	calponin 1, basic, smooth muscle	CNN1	1264	6
205331_s_at	chromosome 5 open reading frame 19	C5orf19	51308	6
219829_at	integrin beta 1 binding protein (melusin) 2	ITGB1BP2	26548	6
220117_at	zinc finger protein 659	ZNF659	79750	6
235050_at	solute carrier family 2 (facilitated glucose transporter), member 12	SLC2A12	154091	6
222570_at	frequenin homolog (Drosophila)	FREQ	23413	6
203698_s_at	frizzled-related protein	FRZB	2487	6
212730_at	desmuslin	DMN	23336	6

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
203088_at	fibulin 5	FBLN5	10516	6
242269_at	FLJ42875 protein	FLJ42875	440556	6
222043_at	clusterin (complement lysis inhibitor, SP-40,40, sulfated glycoprotein 2,	CLU	1191	6
238751_at	Sorbin and SH3 domain containing 2	ARGBP2	8470	6
235129_at	protein phosphatase 1, regulatory (inhibitor) subunit 1A	PPP1R1A	5502	6
211892_s_at	prostaglandin I2 (prostacyclin) synthase ; prostaglandin I2 (prostacyclin) synthase	PTGIS	5740	6
219728_at	myotilin	MYOT	9499	6
229484_at	protein phosphatase 1J (PP2C domain containing)	PPM1J	333926	6
206187_at	prostaglandin I2 (prostacyclin) receptor (IP)	PTGIR	5739	6
234970_at	membrane targeting (tandem) C2 domain containing 1	MTAC2D1	123036	6
211160_x_at	actinin, alpha 1	ACTN1	87	6
235209_at	RPE-spondin	RPESP	157869	6
202796_at	synaptopodin	SYNPO	11346	6
209488_s_at	RNA binding protein with multiple splicing	RBPMS	11030	6
1553613_s_at	forkhead box C1	FOXC1	2296	6
232017_at	tight junction protein 2 (zona occludens 2)	TJP2	9414	6
202274_at	actin, gamma 2, smooth muscle, enteric	ACTG2	72	6
229799_s_at	neural cell adhesion molecule 1	NCAM1	4684	6
223612_s_at	ligand of numb-protein X	LNX	84708	6
204627_s_at	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	ITGB3	3690	6
202566_s_at	supervillin	SVIL	6840	6
214121_x_at	PDZ and LIM domain 7 (enigma)	PDLIM7	9260	6
244419_at	Frizzled-related protein	FRZB	2487	6

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
233546_at	Hypothetical protein LOC283075	LOC283075	283075	6
203238_s_at	Notch homolog 3 (Drosophila)	NOTCH3	4854	6
209244_s_at	kinesin family member 1C	KIF1C	10749	6
227427_at	RAC/CDC42 exchange factor	GEFT	115557	6
209070_s_at	regulator of G-protein signalling 5	RGS5	8490	6
206498_at	oculocutaneous albinism II (pink-eye dilution homolog, mouse)	OCA2	4948	6
227202_at	Contactin 1	CNTN1	1272	6
212848_s_at	chromosome 9 open reading frame 3	C9orf3	84909	6
212823_s_at	pleckstrin homology domain containing, family G (with RhoGef domain) member 3	PLEKHG3	26030	6
242736_at	Sorbin and SH3 domain containing 1	SORBS1	10580	6
213746_s_at	filamin A, alpha (actin binding protein 280)	FLNA	2316	6
206832_s_at	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3F	SEMA3F	6405	6
213714_at	calcium channel, voltage-dependent, beta 2 subunit	CACNB2	783	6
207326_at	betacellulin	BTC	685	6
218892_at	dachsous 1 (Drosophila)	DCHS1	8642	6
204151_x_at	aldo-keto reductase family 1, member C1	AKR1C1	1645	6
214053_at	V-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	ERBB4	2066	6
223842_s_at	scavenger receptor class A, member 3	SCARA3	51435	6
224049_at	potassium channel, subfamily K, member 17	KCNK17	89822	6
235874_at	protease, serine, 35	PRSS35	167681	5
229405_at	kinesin family member 7	KIF7	374654	5
214752_x_at	filamin A, alpha (actin binding protein 280)	FLNA	2316	5
235210_s_at	RPE-spondin	RPESP	157869	5
210605_s_at	milk fat globule-EGF factor 8 protein	MFGE8	4240	5

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
241834_at	Small nuclear ribonucleoprotein polypeptide N	SNRPN	6638	5
227400_at	nuclear factor I/X (CCAAT-binding transcription factor)	NFIX	4784	5
201674_s_at	A kinase (PRKA) anchor protein 1	AKAP1	8165	5
208637_x_at	actinin, alpha 1	ACTN1	87	5
218266_s_at	frequenin homolog (Drosophila)	FREQ	23413	5
238165_at	PDZ domain containing RING finger 3	PDZRN3	23024	5
233974_s_at	chromosome 9 open reading frame 88	C9orf88	64855	5
206243_at	TIMP metallopeptidase inhibitor 4	TIMP4	7079	5
213744_at	attractin-like 1	ATRNL1	26033	5
231851_at	hypothetical protein FLJ10770	RAVER2	55225	5
209082_s_at	collagen, type XVIII, alpha 1	COL18A1	80781	5
204306_s_at	CD151 antigen	CD151	977	5
201262_s_at	biglycan	BGN	633	5
211141_s_at	CCR4-NOT transcription complex, subunit 3	CNOT3	4849	5
225258_at	filamin binding LIM protein 1	FBLIM1	54751	5
222772_at	myelin expression factor 2	MYEF2	50804	5
1557380_at	KIAA1975 protein similar to MRIP2	KIAA1975	119385	5
221845_s_at	ClpB caseinolytic peptidase B homolog (E. coli)	CLPB	81570	5
202565_s_at	supervillin	SVIL	6840	5
214520_at	forkhead box C2 (MFH-1, mesenchyme forkhead 1)	FOXC2	2303	5
1552455_at	chromosome 9 open reading frame 65	C9orf65	158471	5
212554_at	CAP, adenylate cyclase-associated protein, 2 (yeast)	CAP2	10486	5
1552649_a_at	ring finger and FYVE-like domain containing 1	RFFL	117584	5

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
227827_at	Sorbin and SH3 domain containing 2	ARGBP2	8470	5
1553175_s_at	phosphodiesterase 5A, cGMP-specific	PDE5A	8654	5
227826_s_at	Sorbin and SH3 domain containing 2	ARGBP2	8470	5
220334_at	regulator of G-protein signalling 17	RGS17	26575	5
225381_at	hypothetical gene supported by BX647608	LOC399959	399959	5
205236_x_at	superoxide dismutase 3, extracellular	SOD3	6649	5
40524_at	protein tyrosine phosphatase, non-receptor type 21	PTPN21	11099	5
1569290_s_at	glutamate receptor, ionotrophic, AMPA 3	GRIA3	2892	5
1568760_at	myosin, heavy polypeptide 11, smooth muscle	MYH11	4629	5
205384_at	FXYD domain containing ion transport regulator 1 (phospholemman)	FXYD1	5348	5
204337_at	regulator of G-protein signalling 4	RGS4	5999	5
219685_at	transmembrane protein 35	TMEM35	59353	5
204163_at	elastin microfibril interfacer 1	EMILIN1	11117	5
211380_s_at	protein kinase, cGMP-dependent, type I	PRKG1	5592	5
206320_s_at	SMAD, mothers against DPP homolog 9 (Drosophila)	SMAD9	4093	5
221214_s_at	nasal embryonic LHRH factor	NELF	26012	5
236300_at	Phosphodiesterase 3A, cGMP-inhibited	PDE3A	5139	5
220676_at	ADAM metallopeptidase with thrombospondin type 1 motif, 8	ADAMTS8	11095	5
215913_s_at	GULP, engulfment adaptor PTB domain containing 1	GULP1	51454	5
205208_at	aldehyde dehydrogenase 1 family, member L1	ALDH1L1	10840	5
226303_at	phosphoglucomutase 5	PGM5	5239	5
206078_at	kalirin, RhoGEF kinase	KALRN	8997	5
239764_at	hypothetical LOC401048	LOC401048	401048	5
239443_at	protocadherin beta 6	PCDHB6	56130	5
211382_s_at	transforming, acidic coiled-coil containing protein 2	TACC2	10579	5

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
226552_at	immediate early response 5-like	IER5L	389792	5
212713_at	microfibrillar-associated protein 4	MFAP4	4239	5
207542_s_at	aquaporin 1 (channel-forming integral protein, 28kDa)	AQP1	358	5
209160_at	aldo-keto reductase family 1, member C3 (3-alpha hydroxysteroid dehydrogenase, type II)	AKR1C3	8644	5
228816_at	hypothetical protein LOC92270	LOC92270	92270	5
231361_at	Neuroligin 1	NLGN1	22871	5
238983_at	hypothetical protein FLJ14001	FLJ14001	79730	5
91703_at	EH domain binding protein 1-like 1	EHBP1L1	254102	5
207836_s_at	RNA binding protein with multiple splicing	RBPMS	11030	5
210702_s_at	prostaglandin I2 (prostacyclin) synthase	PTGIS	5740	5
214162_at	hypothetical protein LOC284244	LOC284244	284244	5
208491_s_at	phosphoglucomutase 5	PGM5	5239	5
212757_s_at	calcium/calmodulin-dependent protein kinase (CaM kinase) II gamma	CAMK2G	818	5
227253_at	Hermansky-Pudlak syndrome 3 ; Ceruloplasmin (ferroxidase)	HPS3 ; CP	1356 ; 84343	5
204505_s_at	erythrocyte membrane protein band 4.9 (dematin)	EPB49	2039	5
205002_at	AT hook, DNA binding motif, containing 1	AHDC1	27245	5
228507_at	Phosphodiesterase 3A, cGMP-inhibited	PDE3A	5139	5
204288_s_at	sorbin and SH3 domain containing 2	SORBS2	8470	5
202729_s_at	latent transforming growth factor beta binding protein 1	LTBP1	4052	5
204041_at	monoamine oxidase B	MAOB	4129	5
218935_at	EH-domain containing 3	EHD3	30845	5
203662_s_at	tropomodulin 1	TMOD1	7111	5
212944_at	Mitochondrial ribosomal protein S6	MRPS6	64968	5
218820_at	chromosome 14 open reading frame 132	C14orf132	56967	5

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
232734_at	tetratricopeptide repeat domain 23	TTC23	64927	5
202613_at	CTP synthase	CTPS	1503	5
210299_s_at	four and a half LIM domains 1	FHL1	2273	5
232676_x_at	myelin expression factor 2	MYEF2	50804	5
203571_s_at	chromosome 10 open reading frame 116	C10orf116	10974	5
238323_at	TEA domain family member 2	TEAD2	8463	5
235737_at	thymic stromal lymphopoietin	TSLP	85480	5
208791_at	clusterin (complement lysis inhibitor)	CLU	1191	5
226966_at	Huntingtin interacting protein C	HYPC	25766	5
227662_at	synaptopodin 2	SYNPO2	171024	5
218730_s_at	osteoglycin (osteoinductive factor, mimecan)	OGN	4969	5
222921_s_at	hairy/enhancer-of-split related with YRPW motif 2	HEY2	23493	5
216080_s_at	fatty acid desaturase 3	FADS3	3995	5
203986_at	genethonin 1	GENX-3414	8987	5
207876_s_at	filamin C, gamma (actin binding protein 280)	FLNC	2318	5
242935_at	SET binding factor 2	SBF2	81846	5
200859_x_at	filamin A, alpha (actin binding protein 280)	FLNA	2316	5
223629_at	protocadherin beta 5	PCDHB5	26167	5
207554_x_at	thromboxane A2 receptor	TBXA2R	6915	5
204428_s_at	lecithin-cholesterol acyltransferase	LCAT	3931	5
232570_s_at	ADAM metallopeptidase domain 33	ADAM33	80332	5
223321_s_at	fibroblast growth factor receptor-like 1	FGFRL1	53834	5
228388_at	nuclear factor of kappa light polypeptide gene enhancer in B-cells inhibitor, beta	NFKBIB	4793	5
61297_at	CASK interacting protein 2	CASKIN2	57513	5

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
217788_s_at	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2)	GALNT2	2590	5
223475_at	cysteine-rich secretory protein LCCL domain containing 1	CRISPLD1	83690	5
218418_s_at	ankyrin repeat domain 25	ANKRD25	25959	5
203516_at	syntrophin, alpha 1 (dystrophin-associated protein A1, 59kDa, acidic component)	SNTA1	6640	5
233882_s_at	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6D	SEMA6D	80031	5
212062_at	ATPase, Class II, type 9A	ATP9A	10079	5
223749_at	C1q and tumor necrosis factor related protein 2	C1QTNF2	114898	5
212336_at	erythrocyte membrane protein band 4.1-like 1	EPB41L1	2036	5
211340_s_at	melanoma cell adhesion molecule	MCAM	4162	4
228310_at	enabled homolog (Drosophila)	ENAH	55740	4
204773_at	interleukin 11 receptor, alpha	IL11RA	3590	4
1555483_x_at	filamin binding LIM protein 1	FBLIM1	54751	4
213381_at	Chromosome 10 open reading frame 72	C10orf72	196740	4
823_at	chemokine (C-X3-C motif) ligand 1	CX3CL1	6376	4
1559840_s_at	T-box 18	TBX18	9096	4
201058_s_at	myosin, light polypeptide 9, regulatory	MYL9	10398	4
209832_s_at	DNA replication factor	CDT1	81620	4
201234_at	integrin-linked kinase	ILK	3611	4
227439_at	E2a-Pbx1-associated protein	EB-1	56899	4
236372_at	Pannexin 1	PANX1	24145	4
202821_s_at	LIM domain containing preferred translocation partner in lipoma	LPP	4026	4
217025_s_at	drebrin 1	DBN1	1627	4
213205_s_at	KIAA0809 protein	SRISNF2L	23132	4
217966_s_at	chromosome 1 open reading frame 24	C1orf24	116496	4
230933_at	Destrin (actin depolymerizing factor)	DSTN	11034	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
206813_at	cardiotrophin 1	CTF1	1489	4
205577_at	phosphorylase, glycogen; muscle (McArdle syndrome, glycogen storage disease type V)	PYGM	5837	4
209928_s_at	musculin (activated B-cell factor-1)	MSC	9242	4
228890_at	atonal homolog 8 (Drosophila)	ATOH8	84913	4
219882_at	tubulin tyrosine ligase-like family, member 7	TTLL7	79739	4
240088_at	phosphodiesterase 5A, cGMP-specific	PDE5A	8654	4
221583_s_at	potassium large conductance calcium-activated channel, subfamily M, alpha member 1	KCNMA1	3778	4
218062_x_at	CDC42 effector protein (Rho GTPase binding) 4	CDC42EP4	23580	4
1555270_a_at	Wolfram syndrome 1 (wolframin)	WFS1	7466	4
234980_at	Transmembrane protein 56	FLJ31842	148534	4
212669_at	calcium/calmodulin-dependent protein kinase (CaM kinase) II gamma	CAMK2G	818	4
201841_s_at	heat shock 27kDa protein 1	HSPB1	3315	4
213547_at	cullin-associated and neddylation-dissociated 2 (putative)	CAND2	23066	4
206012_at	left-right determination factor 2	LEFTY2	7044	4
221870_at	EH-domain containing 2	EHD2	30846	4
218353_at	regulator of G-protein signalling 5	RGS5	8490	4
229975_at	Bone morphogenetic protein receptor, type IB	BMPR1B	658	4
239480_at	Glutamate receptor, metabotropic 3	GRM3	2913	4
203498_at	Down syndrome critical region gene 1-like 1	DSCR1L1	10231	4
221748_s_at	tensin 1 ; tensin 1	TNS1	7145	4
205117_at	fibroblast growth factor 1 (acidic)	FGF1	2246	4
204083_s_at	tropomyosin 2 (beta)	TPM2	7169	4
1552760_at	histone deacetylase 9	HDAC9	9734	4
218824_at	hypothetical protein FLJ10781	FLJ10781	55228	4
230146_s_at	frequenin homolog (Drosophila)	FREQ	23413	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
1556096_s_at	unc-13 homolog C (C. elegans)	UNC13C	440279	4
226018_at	hypothetical protein Ells1	Ells1	222166	4
224919_at	mitochondrial ribosomal protein S6	MRPS6	64968	4
1553132_a_at	membrane targeting (tandem) C2 domain containing 1	MTAC2D1	123036	4
212091_s_at	collagen, type VI, alpha 1	COL6A1	1291	4
243209_at	potassium voltage-gated channel, KQT-like subfamily, member 4	KCNQ4	9132	4
212518_at	phosphatidylinositol-4-phosphate 5-kinase, type I, gamma	PIP5K1C	23396	4
214212_x_at	pleckstrin homology domain containing, family C (with FERM domain) member 1	PLEKHC1	10979	4
226207_at	hypothetical protein FLJ39378	FLJ39378	353116	4
211126_s_at	cysteine and glycine-rich protein 2	CSRP2	1466	4
235128_at	synaptopodin	SYNPO	11346	4
226360_at	zinc and ring finger 3	ZNRF3	84133	4
221974_at	Small nuclear ribonucleoprotein polypeptide N	SNRPN	6638	4
210941_at	BH-protocadherin (brain-heart)	PCDH7	5099	4
40489_at	atrophin 1	ATN1	1822	4
1558034_s_at	ceruloplasmin (ferroxidase)	CP	1356	4
205295_at	creatine kinase, mitochondrial 2 (sarcomeric)	CKMT2	1160	4
207030_s_at	cysteine and glycine-rich protein 2	CSRP2	1466	4
205952_at	potassium channel, subfamily K, member 3	KCNK3	3777	4
227236_at	tetraspanin 2	TSPAN2	10100	4
210935_s_at	WD repeat domain 1	WDR1	9948	4
219093_at	hypothetical protein FLJ20701 ; hypothetical protein FLJ20701	FLJ20701	55022	4
229464_at	myelin expression factor 2	MYEF2	50804	4
226408_at	TEA domain family member 2	TEAD2	8463	4
1553194_at	neuronal growth regulator 1	NEGR1	257194	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
222722_at	osteoglycin (osteoinductive factor, mimecan)	OGN	4969	4
202222_s_at	desmin	DES	1674	4
220595_at	PDZ domain containing RING finger 4	PDZRN4	29951	4
211323_s_at	inositol 1,4,5-triphosphate receptor, type 1	ITPR1	3708	4
236584_at	chromosome 1 open reading frame 86	C1orf86	199990	4
212567_s_at	microtubule-associated protein 4	MAP4	4134	4
217728_at	S100 calcium binding protein A6 (calcyclin)	S100A6	6277	4
207837_at	RNA binding protein with multiple splicing	RBPMS	11030	4
227248_at	hypothetical protein FLJ21019	FLJ21019	79990	4
233487_s_at	leucine rich repeat containing 8 family, member A	LRRC8A	56262	4
209071_s_at	regulator of G-protein signalling 5	RGS5	8490	4
238583_at	methionine sulfoxide reductase B3	MSRB3	253827	4
209262_s_at	nuclear receptor subfamily 2, group F, member 6	NR2F6	2063	4
219327_s_at	G protein-coupled receptor, family C, group 5, member C	GPRC5C	55890	4
202289_s_at	transforming, acidic coiled-coil containing protein 2	TACC2	10579	4
225728_at	Importin 9	IPO9	55705	4
231386_at	FLJ30851 protein	FLJ30851	375190	4
204749_at	nucleosome assembly protein 1-like 3	NAP1L3	4675	4
221755_at	EH domain binding protein 1-like 1	EHBP1L1	254102	4
1557223_at	RNA binding protein with multiple splicing	RBPMS	11030	4
228277_at	F-box and leucine-rich repeat protein 19	FBXL19	54620	4
218675_at	solute carrier family 22 (organic cation transporter), member 17	SLC22A17	51310	4
201868_s_at	transducin (beta)-like 1X-linked	TBL1X	6907	4
204693_at	CDC42 effector protein (Rho GTPase binding) 1	CDC42EP1	11135	4
224663_s_at	cofilin 2 (muscle)	CFL2	1073	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
200879_s_at	endothelial PAS domain protein 1	EPAS1	2034	4
229890_at	proline-rich transmembrane protein 1	PRRT1	80863	4
237515_at	Transmembrane protein 56	FLJ31842	148534	4
207159_x_at	mucoepidermoid carcinoma translocated 1	MECT1	23373	4
208937_s_at	inhibitor of DNA binding 1, dominant negative helix-loop-helix protein	ID1	3397	4
204669_s_at	ring finger protein 24	RNF24	11237	4
209651_at	transforming growth factor beta 1 induced transcript 1	TGFB1I1	7041	4
224976_at	nuclear factor I/A	NFIA	4774	4
211573_x_at	transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)	TGM2	7052	4
213974_at	ADAMTS-like 3	ADAMTSL3	57188	4
225342_at	adenylate kinase 3-like 1	AK3L1	205	4
201675_at	A kinase (PRKA) anchor protein 1	AKAP1	8165	4
208889_s_at	nuclear receptor co-repressor 2	NCOR2	9612	4
201801_s_at	solute carrier family 29 (nucleoside transporters), member 1	SLC29A1	2030	4
204348_s_at	adenylate kinase 3-like 1	AK3L1	205	4
215506_s_at	DIRAS family, GTP-binding RAS-like 3	DIRAS3	9077	4
207336_at	SRY (sex determining region Y)-box 5	SOX5	6660	4
201604_s_at	protein phosphatase 1, regulatory (inhibitor) subunit 12A	PPP1R12A	4659	4
227945_at	TBC1 (tre-2/USP6, BUB2, cdc16) domain family, member 1	TBC1D1	23216	4
206117_at	tropomyosin 1 (alpha)	TPM1	7168	4
228988_at	zinc finger protein 6 (CMPX1)	ZNF6	7552	4
204944_at	protein tyrosine phosphatase, receptor type, G	PTPRG	5793	4
213497_at	ankyrin repeat and BTB (POZ) domain containing 2	ABTB2	25841	4
204235_s_at	GULP, engulfment adaptor PTB domain containing 1	GULP1	51454	4
219377_at	family with sequence similarity 59, member A	FAM59A	64762	4
215692_s_at	metallophosphoesterase domain containing 2	MPPED2	744	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
227272_at	FLJ43339 protein	FLJ43339	388115	4
209209_s_at	pleckstrin homology domain containing, family C (with FERM domain) member 1	PLEKHC1	10979	4
242734_x_at	galactose-1-phosphate uridylyltransferase	GALT	2592	4
219609_at	WD repeat domain 25	WDR25	79446	4
1555269_a_at	transmembrane protein 16A	TMEM16A	55107	4
205534_at	BH-protocadherin (brain-heart)	PCDH7	5099	4
234068_s_at	adaptor-related protein complex 2, alpha 1 subunit	AP2A1	160	4
1554126_at	methionine sulfoxide reductase B3	MSRB3	253827	4
239744_at	Regulator of G-protein signalling 3	RGS3	5998	4
231131_at	hypothetical protein FLJ37659	RP1-32F7.2	286499	4
208430_s_at	dystrobrevin, alpha	DTNA	1837	4
209243_s_at	paternally expressed 3	PEG3	5178	4
223853_at	blood vessel epicardial substance	BVES	11149	4
218974_at	hypothetical protein FLJ10159	FLJ10159	55084	4
211347_at	CDC14 cell division cycle 14 homolog B (S. cerevisiae)	CDC14B	8555	4
204894_s_at	amine oxidase, copper containing 3 (vascular adhesion protein 1)	AOC3	8639	4
230360_at	gliomedin	GLDN	342035	4
227702_at	cytochrome P450, family 4, subfamily X, polypeptide 1	CYP4X1	260293	4
214875_x_at	amyloid beta (A4) precursor-like protein 2	APLP2	334	4
219369_s_at	OTU domain, ubiquitin aldehyde binding 2	OTUB2	78990	4
212338_at	myosin ID	MYO1D	4642	4
222664_at	potassium channel tetramerisation domain containing 15	KCTD15	79047	4
216352_x_at	protocadherin gamma subfamily A, 3	PCDHGA3	56112	4
209487_at	RNA binding protein with multiple splicing	RBPMS	11030	4
212328_at	KIAA1102 protein	KIAA1102	22998	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
205579_at	histamine receptor H1	HRH1	3269	4
203661_s_at	tropomodulin 1	TMOD1	7111	4
206973_at	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF)	PPFIA2	8499	4
1554640_at	paralemmin 2	PALM2	114299	4
228967_at	Eukaryotic translation initiation factor 1	SUI1	10209	4
220975_s_at	C1q and tumor necrosis factor related protein 1 ; C1q and tumor necrosis factor related protein 1	C1QTNF1	114897	4
237329_at	hypothetical LOC389100	LOC389100	389100	4
232806_s_at	hypothetical protein MGC21688	MGC21688	131408	4
213924_at	Metallophosphoesterase 1	MPPE1	65258	4
228213_at	H2A histone family, member J	H2AFJ	55766	4
204657_s_at	Src homology 2 domain containing adaptor protein B	SHB	6461	4
202709_at	fibromodulin	FMOD	2331	4
204321_at	neogenin homolog 1 (chicken)	NEO1	4756	4
202908_at	Wolfram syndrome 1 (wolframin)	WFS1	7466	4
233167_at	selenoprotein O	SELO	83642	4
209951_s_at	mitogen-activated protein kinase kinase 7	MAP2K7	5609	4
209098_s_at	jagged 1 (Alagille syndrome)	JAG1	182	4
214027_x_at	desmin ; family with sequence similarity 48, member A	DES ; FAM48A	1674 ; 55578	4
222101_s_at	dachsous 1 (Drosophila)	DCHS1	8642	4
238514_at	transmembrane protein 25	TMEM25	84866	4
33850_at	microtubule-associated protein 4	MAP4	4134	4
204939_s_at	phospholamban	PLN	5350	4
202401_s_at	serum response factor (c-fos serum response element-binding transcription factor)	SRF	6722	4
205120_s_at	sarcoglycan, beta (43kDa dystrophin-associated glycoprotein)	SGCB	6443	4
39549_at	neuronal PAS domain protein 2	NPAS2	4862	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
202822_at	LIM domain containing preferred translocation partner in lipoma	LPP	4026	4
221088_s_at	protein phosphatase 1, regulatory (inhibitor) subunit 9A	PPP1R9A	55607	4
225270_at	neogenin homolog 1 (chicken)	NEO1	4756	4
227297_at	Integrin, alpha 9	ITGA9	3680	4
226814_at	ADAM metallopeptidase with thrombospondin type 1 motif, 9	ADAMTS9	56999	4
229034_at	hypothetical protein FLJ10159	FLJ10159	55084	4
212361_s_at	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	ATP2A2	488	4
202054_s_at	aldehyde dehydrogenase 3 family, member A2	ALDH3A2	224	4
243_g_at	microtubule-associated protein 4	MAP4	4134	4
212473_s_at	microtubule associated monoxygenase, calponin and LIM domain containing 2	MICAL2	9645	4
219218_at	KIAA1447 protein	KIAA1447	57597	4
201681_s_at	discs, large homolog 5 (Drosophila)	DLG5	9231	4
209293_x_at	inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	ID4	3400	4
214322_at	calcium/calmodulin-dependent protein kinase (CaM kinase) II gamma	CAMK2G	818	4
214721_x_at	CDC42 effector protein (Rho GTPase binding) 4	CDC42EP4	23580	4
213164_at	solute carrier family 5 (inositol transporters), member 3	SLC5A3	6526	4
221884_at	ecotropic viral integration site 1	EVI1	2122	4
226926_at	dermokine	ZD52F10	93099	4
227506_at	solute carrier family 16 (monocarboxylic acid transporters), member 9	SLC16A9	220963	4
212325_at	KIAA1102 protein	KIAA1102	22998	4
228143_at	ceruloplasmin (ferroxidase)	CP	1356	4
49051_g_at	deltex 3 homolog (Drosophila)	DTX3	196403	4
212573_at	KIAA0830 protein	KIAA0830	23052	4
218843_at	fibronectin type III domain containing 4	FNDC4	64838	4
213010_at	protein kinase C, delta binding protein	PRKCDBP	112464	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
222433_at	enabled homolog (Drosophila)	ENAH	55740	4
213447_at	imprinted in Prader-Willi syndrome	IPW	3653	4
207069_s_at	SMAD, mothers against DPP homolog 6 (Drosophila)	SMAD6	4091	4
208874_x_at	protein phosphatase 2A, regulatory subunit B' (PR 53)	PPP2R4	5524	4
225078_at	epithelial membrane protein 2	EMP2	2013	4
205076_s_at	myotubularin related protein 11	MTMR11	10903	4
227644_at	regulating synaptic membrane exocytosis 4	RIMS4	140730	4
216867_s_at	platelet-derived growth factor alpha polypeptide	PDGFA	5154	4
219733_s_at	solute carrier family 27 (fatty acid transporter), member 5	SLC27A5	10998	4
226884_at	leucine rich repeat neuronal 1	LRRN1	57633	4
224970_at	nuclear factor I/A	NFIA	4774	4
218045_x_at	parathymosin	PTMS	5763	4
219509_at	myozenin 1	MYOZ1	58529	4
204237_at	GULP, engulfment adaptor PTB domain containing 1	GULP1	51454	4
223495_at	coiled-coil domain containing 8	CCDC8	83987	4
229063_s_at	hypothetical protein MGC31967	MGC31967	203260	4
227392_at	nischarin	NISCH	11188	4
210706_s_at	ring finger protein 24	RNF24	11237	4
220825_s_at	kin of IRRE like (Drosophila)	KIRREL	55243	4
222434_at	enabled homolog (Drosophila)	ENAH	55740	4
204570_at	cytochrome c oxidase subunit VIIa polypeptide 1 (muscle)	COX7A1	1346	4
205397_x_at	SMAD, mothers against DPP homolog 3 (Drosophila)	SMAD3	4088	4
204257_at	fatty acid desaturase 3	FADS3	3995	4
226518_at	potassium channel tetramerisation domain containing 10	KCTD10	83892	4
227084_at	dystrobrevin, alpha	DTNA	1837	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
202555_s_at	myosin, light polypeptide kinase ; myosin, light polypeptide kinase	MYLK	4638	4
227699_at	chromosome 14 open reading frame 149	C14orf149	112849	4
217967_s_at	chromosome 1 open reading frame 24	C1orf24	116496	4
213541_s_at	v-ets erythroblastosis virus E26 oncogene like (avian)	ERG	2078	4
227328_at	Calmodulin binding transcription activator 1	CAMTA1	23261	4
216272_x_at	synapse defective 1, Rho GTPase, homolog 1 (C. elegans)	SYDE1	85360	4
203441_s_at	cadherin 2, type 1, N-cadherin (neuronal)	CDH2	1000	4
201559_s_at	chloride intracellular channel 4	CLIC4	25932	4
225020_at	DAB2 interacting protein	DAB2IP	153090	4
237116_at	Profilin 2	PFN2	5217	4
227848_at	phosphatidylethanolamine-binding protein 4	PEBP4	157310	4
206306_at	ryanodine receptor 3	RYR3	6263	4
235108_at	Potassium channel, subfamily K, member 3	KCNK3	3777	4
210625_s_at	A kinase (PRKA) anchor protein 1	AKAP1	8165	4
202834_at	angiotensinogen (serpin peptidase inhibitor, clade A, member 8)	AGT	183	4
211538_s_at	heat shock 70kDa protein 2	HSPA2	3306	4
212937_s_at	collagen, type VI, alpha 1	COL6A1	1291	4
233498_at	V-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	ERBB4	2066	4
228984_at	KIAA1394 protein	KIAA1394	57571	4
1553672_at	enabled homolog (Drosophila)	ENAH	55740	4
201173_x_at	nuclear distribution gene C homolog (A. nidulans)	NUDC	10726	4
40850_at	FK506 binding protein 8, 38kDa	FKBP8	23770	4
233496_s_at	cofilin 2 (muscle)	CFL2	1073	4
204004_at	PRKC, apoptosis, WT1, regulator	PAWR	5074	4
224057_s_at	THAP domain containing 4	THAP4	51078	4

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
213283_s_at	sal-like 2 (Drosophila)	SALL2	6297	4
202928_s_at	PHD finger protein 1	PHF1	5252	4
212564_at	potassium channel tetramerisation domain containing 2	KCTD2	23510	4
200621_at	cysteine and glycine-rich protein 1	CSRP1	1465	4
235497_at	Hypothetical protein LOC284591	LOC284591	284591	4
211110_s_at	androgen receptor	AR	367	4
242545_at	tubulin tyrosine ligase-like family, member 11	TTLL11	158135	4
205717_x_at	protocadherin gamma subfamily C, 3	PCDHGC3	26025	4
229774_at	CXXC finger 4	CXXC4	80319	4
1554574_a_at	cytochrome b5 reductase 3	CYB5R3	1727	4
221656_s_at	Rho guanine nucleotide exchange factor (GEF) 10-like	ARHGEF10L	55160	4
208682_s_at	melanoma antigen family D, 2	MAGED2	10916	4
201497_x_at	myosin, heavy polypeptide 11, smooth muscle	MYH11	4629	4
204992_s_at	profilin 2	PFN2	5217	4
232235_at	chromosome 18 open reading frame 4	C18orf4	92126	4
209633_at	protein phosphatase 2 (formerly 2A), regulatory subunit B", alpha	PPP2R3A	5523	4
220617_s_at	zinc finger protein 532	ZNF532	55205	4
223496_s_at	coiled-coil domain containing 8	CCDC8	83987	4
209896_s_at	protein tyrosine phosphatase, non-receptor type 11 (Noonan syndrome 1)	PTPN11	5781	4
225380_at	hypothetical protein BC007901	LOC91461	91461	4
1554784_at	contactin 1	CNTN1	1272	4
204036_at	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 2	EDG2	1902	4
226856_at	musculoskeletal, embryonic nuclear protein 1	MUSTN1	389125	4
205934_at	phospholipase C-like 1	PLCL1	5334	3
232406_at	Jagged 1 (Alagille syndrome)	JAG1	182	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
221408_x_at	protocadherin beta 12	PCDHB12	56124	3
215306_at	Luteinizing hormone/choriogonadotropin receptor	LHCGR	3973	3
201869_s_at	transducin (beta)-like 1X-linked	TBL1X	6907	3
208760_at	Ubiquitin-conjugating enzyme E2I (UBC9 homolog, yeast)	UBE2I	7329	3
222406_s_at	proline-rich nuclear receptor coactivator 2	PNRC2	55629	3
235721_at	deltex 3 homolog (Drosophila)	DTX3	196403	3
212372_at	myosin, heavy polypeptide 10, non-muscle	MYH10	4628	3
203550_s_at	chromosome 1 open reading frame 2	C1orf2	10712	3
205231_s_at	epilepsy, progressive myoclonus type 2A, Lafora disease (laforin)	EPM2A	7957	3
220936_s_at	H2A histone family, member J	H2AFJ	55766	3
209656_s_at	transmembrane protein 47	TMEM47	83604	3
231721_at	junctional adhesion molecule 3	JAM3	83700	3
224352_s_at	cofilin 2 (muscle) ; cofilin 2 (muscle)	CFL2	1073	3
226388_at	transcription elongation factor A (SII), 3	TCEA3	6920	3
201554_x_at	glycogenin	GYG	2992	3
201467_s_at	NAD(P)H dehydrogenase, quinone 1	NQO1	1728	3
212003_at	chromosome 1 open reading frame 144	C1orf144	26099	3
242064_at	sidekick homolog 2 (chicken)	SDK2	54549	3
214282_at	Ceruloplasmin (ferroxidase)	CP	1356	3
204099_at	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily d, member 3	SMARCD3	6604	3
221628_s_at	cytokine-like nuclear factor n-pac	N-PAC	84656	3
203425_s_at	insulin-like growth factor binding protein 5	IGFBP5	3488	3
207968_s_at	MADS box transcription enhancer factor 2, polypeptide C (myocyte enhancer factor 2C)	MEF2C	4208	3
229504_at	RAB23, member RAS oncogene family	RAB23	51715	3
1570515_a_at	filamin A interacting protein 1	FILIP1	27145	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
224798_s_at	chromosome 15 open reading frame 17	C15orf17	57184	3
227083_at	beta 3-glycosyltransferase-like	B3GTL	145173	3
204485_s_at	target of myb1-like 1 (chicken)	TOM1L1	10040	3
1560407_at	MAP/microtubule affinity-regulating kinase 1	MARK1	4139	3
202815_s_at	hexamethylene bis-acetamide inducible 1	HEXIM1	10614	3
242447_at	hypothetical gene supported by AK091454	LOC285382	285382	3
204422_s_at	fibroblast growth factor 2 (basic)	FGF2	2247	3
209195_s_at	adenylate cyclase 6	ADCY6	112	3
201616_s_at	caldesmon 1	CALD1	800	3
210317_s_at	tyrosine 3-monooxygenase/tryptophan 5-monooxygenase activation protein, epsilon polypeptide	YWHAE	7531	3
202085_at	tight junction protein 2 (zona occludens 2)	TJP2	9414	3
227326_at	matrix-remodelling associated 7	MXRA7	439921	3
239763_at	PR domain containing 11	PRDM11	56981	3
231336_at	copine IV	CPNE4	131034	3
203881_s_at	dystrophin (muscular dystrophy, Duchenne and Becker types)	DMD	1756	3
228625_at	Cbp/p300-interacting transactivator, with Glu/Asp-rich carboxy-terminal domain, 4	CITED4	163732	3
212437_at	centromere protein B, 80kDa	CENPB	1059	3
208704_x_at	amyloid beta (A4) precursor-like protein 2	APLP2	334	3
219922_s_at	latent transforming growth factor beta binding protein 3	LTBP3	4054	3
213627_at	melanoma antigen family D, 2	MAGED2	10916	3
204037_at	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 2	EDG2	1902	3
1569149_at	PDZ and LIM domain 7 (enigma)	PDLIM7	9260	3
204396_s_at	G protein-coupled receptor kinase 5	GRK5	2869	3
205429_s_at	membrane protein, palmitoylated 6 (MAGUK p55 subfamily member 6)	MPP6	51678	3
215294_s_at	SWI/SNF related, matrix associated, actin dependent regulator subfamily	SMARCA1	6594	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
209454_s_at	TEA domain family member 3	TEAD3	7005	3
213906_at	v-myb myeloblastosis viral oncogene homolog (avian)-like 1	MYBL1	4603	3
45297_at	EH-domain containing 2	EHD2	30846	3
218780_at	hook homolog 2 (Drosophila)	HOOK2	29911	3
224458_at	chromosome 9 open reading frame 125 ; chromosome 9 open reading frame 125	C9orf125	84302	3
210976_s_at	phosphofructokinase, muscle	PFKM	5213	3
205348_s_at	dynein, cytoplasmic, intermediate polypeptide 1	DNCI1	1780	3
224773_at	neuron navigator 1	NAV1	89796	3
201749_at	Endothelin converting enzyme 1	ECE1	1889	3
208871_at	atrophin 1	ATN1	1822	3
212803_at	NGFI-A binding protein 2 (EGR1 binding protein 2)	NAB2	4665	3
209015_s_at	DnaJ (Hsp40) homolog, subfamily B, member 6	DNAJB6	10049	3
215324_at	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3D	SEMA3D	223117	3
203733_at	dexamethasone-induced transcript	DEXI	28955	3
205111_s_at	phospholipase C, epsilon 1	PLCE1	51196	3
229095_s_at	LIM and senescent cell antigen-like domains 3	LIMS3	96626	3
203464_s_at	epsin 2	EPN2	22905	3
215505_s_at	striatin, calmodulin binding protein 3	STRN3	29966	3
221584_s_at	potassium large conductance calcium-activated channel, subfamily M, alpha member 1	KCNMA1	3778	3
227120_at	forkhead box P4	FOXP4	116113	3
216234_s_at	protein kinase, cAMP-dependent, catalytic, alpha	PRKACA	5566	3
224995_at	spire homolog 1 (Drosophila)	SPIRE1	56907	3
212680_x_at	protein phosphatase 1, regulatory (inhibitor) subunit 14B	PPP1R14B	26472	3
209789_at	coronin, actin binding protein, 2B	CORO2B	10391	3
207781_s_at	zinc finger protein 6 (CMPX1)	ZNF6	7552	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
205224_at	surfeit 2	SURF2	6835	3
226223_at	PRKC, apoptosis, WT1, regulator	PAWR	5074	3
228737_at	chromosome 20 open reading frame 100	C20orf100	84969	3
212005_at	chromosome 1 open reading frame 144	C1orf144	26099	3
226305_at	Ly6/neurotoxin 1	LYNX1	66004	3
229004_at	ADAM metallopeptidase with thrombospondin type 1 motif, 15	ADAMTS15	170689	3
226188_at	HSPC159 protein	HSPC159	29094	3
218678_at	nestin	NES	10763	3
219451_at	methionine sulfoxide reductase B2	MSRB2	22921	3
213324_at	v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog (avian)	SRC	6714	3
219965_s_at	PDZ domain containing, X chromosome	FLJ21687	79917	3
227099_s_at	hypothetical LOC387763	LOC387763	387763	3
204310_s_at	natriuretic peptide receptor B/guanylate cyclase B (atrionatriuretic peptide receptor B)	NPR2	4882	3
219929_s_at	zinc finger, FYVE domain containing 21	ZFYVE21	79038	3
227875_at	kelch-like 13 (Drosophila)	KLHL13	90293	3
213138_at	AT rich interactive domain 5A (MRF1-like)	ARID5A	10865	3
228306_at	Cornichon homolog 4 (Drosophila)	HSPC163	29097	3
217818_s_at	actin related protein 2/3 complex, subunit 4, 20kDa	ARPC4	10093	3
239657_x_at	forkhead box protein O6	FOXO6	343552	3
211031_s_at	cytoplasmic linker 2 ; cytoplasmic linker 2	CYLN2	7461	3
207012_at	matrix metallopeptidase 16 (membrane-inserted)	MMP16	4325	3
211621_at	androgen receptor (dihydrotestosterone receptor; testicular feminization;	AR	367	3
210967_x_at	calcium channel, voltage-dependent, beta 1 subunit	CACNB1	782	3
1557382_x_at	KIAA1975 protein similar to MRIP2	KIAA1975	119385	3
228162_at	Esterase D/formylglutathione hydrolase	ESD	2098	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
205993_s_at	T-box 2	TBX2	6909	3
212705_x_at	patatin-like phospholipase domain containing 2	PNPLA2	57104	3
211569_s_at	L-3-hydroxyacyl-Coenzyme A dehydrogenase, short chain	HADHSC	3033	3
205450_at	phosphorylase kinase, alpha 1 (muscle)	PHKA1	5255	3
203612_at	bystin-like	BYSL	705	3
202617_s_at	methyl CpG binding protein 2 (Rett syndrome)	MECP2	4204	3
209837_at	adaptor-related protein complex 4, mu 1 subunit	AP4M1	9179	3
210544_s_at	aldehyde dehydrogenase 3 family, member A2	ALDH3A2	224	3
202328_s_at	polycystic kidney disease 1 (autosomal dominant)	PKD1	5310	3
209632_at	protein phosphatase 2 (formerly 2A), regulatory subunit B", alpha	PPP2R3A	5523	3
228933_at	Nance-Horan syndrome (congenital cataracts and dental anomalies)	NHS	4810	3
219179_at	dapper, antagonist of beta-catenin, homolog 1 (Xenopus laevis)	DACT1	51339	3
230161_at	CD99 antigen	CD99	4267	3
221104_s_at	nipsnap homolog 3B (C. elegans)	NIPSNAP3B	55335	3
238021_s_at	hypothetical gene supported by AF275804	LOC388279	388279	3
204135_at	downregulated in ovarian cancer 1	DOC1	11259	3
205279_s_at	glycine receptor, beta	GLRB	2743	3
218204_s_at	FYVE and coiled-coil domain containing 1	FYCO1	79443	3
201468_s_at	NAD(P)H dehydrogenase, quinone 1	NQO1	1728	3
200808_s_at	zyxin	ZYX	7791	3
226500_at	zinc finger protein 651	ZNF651	92999	3
208790_s_at	polymerase I and transcript release factor	PTRF	284119	3
223614_at	hypothetical protein DKFZp761D112	DKFZp761D112	84257	3
244623_at	Transcribed locus			3
1554710_at	potassium large conductance calcium-activated channel, subfamily M, beta member 1	KCNMB1	3779	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
225855_at	erythrocyte membrane protein band 4.1 like 5	EPB41L5	57669	3
232309_at	hypothetical protein LOC202181	LOC202181	202181	3
200931_s_at	vinculin	VCL	7414	3
235759_at	EF-hand calcium binding protein 1	EFCBP1	64168	3
236330_at	CDNA FLJ42688 fis, clone BRAMY3002120			3
218359_at	chromosome 20 open reading frame 98	C20orf98	80023	3
1552521_a_at	transmembrane protein 74	TMEM74	157753	3
219902_at	betaine-homocysteine methyltransferase 2	BHMT2	23743	3
226492_at	sema domain, transmembrane domain (TM), and cytoplasmic domain, (semaphorin) 6D	SEMA6D	80031	3
226542_at	Full-length cDNA clone CS0DJ002YF02 of T cells (Jurkat cell line)			3
217509_x_at	glutamate receptor, ionotropic, kainate 5	GRIK5	2901	3
226411_at	ecotropic viral integration site 5-like	EVI5L	115704	3
204628_s_at	integrin, beta 3 (platelet glycoprotein IIIa, antigen CD61)	ITGB3	3690	3
229335_at	immunoglobulin superfamily, member 4C	IGSF4C	199731	3
209402_s_at	solute carrier family 12 (potassium/chloride transporters), member 4	SLC12A4	6560	3
224894_at	Yes-associated protein 1, 65kDa	YAP1	10413	3
217223_s_at	breakpoint cluster region	BCR	613	3
215247_at	hypothetical protein LOC339692	LOC339692	339692	3
208255_s_at	FK506 binding protein 8, 38kDa	FKBP8	23770	3
1556194_a_at	CDNA clone IMAGE:5285801			3
40093_at	Lutheran blood group (Auberger b antigen included)	LU	4059	3
211404_s_at	amyloid beta (A4) precursor-like protein 2	APLP2	334	3
32094_at	carbohydrate (chondroitin 6) sulfotransferase 3	CHST3	9469	3
204793_at	G protein-coupled receptor associated sorting protein 1	GPRASP1	9737	3
224811_at	CDNA clone IMAGE:5286019			3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
238805_at	similar to RIKEN cDNA 2310030G06 gene	MGC14839	91894	3
209878_s_at	v-rel reticuloendotheliosis viral oncogene homolog A,	RELA	5970	3
225935_at	CDNA clone IMAGE:4769453			3
204472_at	GTP binding protein overexpressed in skeletal muscle	GEM	2669	3
1556129_at	Hypothetical protein FLJ12986	FLJ12986	197319	3
205442_at	microfibrillar-associated protein 3-like	MFAP3L	9848	3
1560537_at	Fibroblast growth factor 13	FGF13	2258	3
225459_at	angiomotin like 1	AMOTL1	154810	3
227034_at	chromosome 2 open reading frame 26	C2orf26	65124	3
222956_at	fidgetin	FIGN	55137	3
226051_at	selenoprotein M	SELM	140606	3
1558152_at	Hypothetical protein MGC3234	MGC3234	66005	3
1558487_a_at	transmembrane emp24 protein transport domain containing 4	TMED4	222068	3
1554783_s_at	rho/rac guanine nucleotide exchange factor (GEF) 2	ARHGEF2	9181	3
220482_s_at	deafness locus associated putative guanine nucleotide exchange factor	DELGEF	26297	3
201332_s_at	signal transducer and activator of transcription 6, interleukin-4 induced	STAT6	6778	3
202336_s_at	peptidylglycine alpha-amidating monooxygenase	PAM	5066	3
1559839_at	T-box 18	TBX18	9096	3
202982_s_at	acyl-CoA thioesterase 2	ACOT2	10965	3
210150_s_at	laminin, alpha 5	LAMA5	3911	3
202032_s_at	mannosidase, alpha, class 2A, member 2	MAN2A2	4122	3
1555240_s_at	guanine nucleotide binding protein (G protein), gamma 12	GNG12	55970	3
225096_at	hypothetical protein, clone 2746033	HSA272196	55352	3
213103_at	START domain containing 13	STARD13	90627	3
203710_at	inositol 1,4,5-triphosphate receptor, type 1	ITPR1	3708	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
208096_s_at	collagen, type XXI, alpha 1 ; collagen, type XXI, alpha 1	COL21A1	81578	3
1557375_at	Ellis van Creveld syndrome	EVC	2121	3
219511_s_at	synuclein, alpha interacting protein (synphilin)	SNCAIP	9627	3
219053_s_at	vacuolar protein sorting 37C (yeast)	VPS37C	55048	3
215515_at	Kin of IRRE like (Drosophila)	KIRREL	55243	3
223681_s_at	InaD-like (Drosophila)	INADL	10207	3
208131_s_at	prostaglandin I2 (prostacyclin) synthase ; prostaglandin I2 (prostacyclin) synthase	PTGIS	5740	3
564_at	guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	3
221566_s_at	nucleolar protein 3 (apoptosis repressor with CARD domain)	NOL3	8996	3
210473_s_at	G protein-coupled receptor 125	GPR125	166647	3
222918_at	RAB9B, member RAS oncogene family	RAB9B	51209	3
201983_s_at	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	EGFR	1956	3
217294_s_at	enolase 1, (alpha)	ENO1	2023	3
218364_at	leucine rich repeat (in FLII) interacting protein 2	LRRFIP2	9209	3
204975_at	epithelial membrane protein 2	EMP2	2013	3
213710_s_at	Calmodulin 1 (phosphorylase kinase, delta)	CALM1	801	3
203722_at	aldehyde dehydrogenase 4 family, member A1	ALDH4A1	8659	3
213181_s_at	molybdenum cofactor synthesis 1	MOCS1	4337	3
211343_s_at	collagen, type XIII, alpha 1	COL13A1	1305	3
1558214_s_at	catenin (cadherin-associated protein), alpha 1, 102kDa	CTNNA1	1495	3
212327_at	KIAA1102 protein	KIAA1102	22998	3
213217_at	adenylate cyclase 2 (brain)	ADCY2	108	3
201120_s_at	progesterone receptor membrane component 1	PGRMC1	10857	3
231118_at	ankyrin repeat domain 35	ANKRD35	148741	3
227679_at	Histone deacetylase 11	HDAC11	79885	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
215706_x_at	zyxin	ZYX	7791	3
212655_at	zinc finger, CCHC domain containing 14	ZCCHC14	23174	3
219670_at	chromosome 1 open reading frame 165	C1orf165	79656	3
200623_s_at	calmodulin 3 (phosphorylase kinase, delta)	CALM3	808	3
226420_at	ecotropic viral integration site 1	EVI1	2122	3
221487_s_at	endosulfine alpha	ENSA	2029	3
212701_at	Talin 2	TLN2	83660	3
210792_x_at	CD27-binding (Siva) protein	SIVA	10572	3
218416_s_at	hypothetical protein FLJ20489	FLJ20489	55652	3
203792_x_at	polycomb group ring finger 2	PCGF2	7703	3
1558295_a_at	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF),	PPFIA2	8499	3
1557910_at	heat shock 90kDa protein 1, beta	HSPCB	3326	3
219011_at	pleckstrin homology domain containing, family A (phosphoinositide binding specific) member 4	PLEKHA4	57664	3
226591_at	Small nuclear ribonucleoprotein polypeptide N	SNRPN	6638	3
208977_x_at	tubulin, beta, 2	TUBB2	10383	3
226763_at	SEC14 and spectrin domains 1	SESTD1	91404	3
216268_s_at	jagged 1 (Alagille syndrome)	JAG1	182	3
234312_s_at	acyl-CoA synthetase short-chain family member 2	ACSS2	55902	3
226071_at	thrombospondin repeat containing 1	TSRC1	54507	3
1554179_s_at	Ly6/neurotoxin 1	LYNX1	66004	3
200836_s_at	microtubule-associated protein 4	MAP4	4134	3
221846_s_at	CASK interacting protein 2	CASKIN2	57513	3
202464_s_at	6-phosphofructo-2-kinase/fructose-2,6-biphosphatase 3	PFKFB3	5209	3
1554127_s_at	methionine sulfoxide reductase B3	MSRB3	253827	3
223482_at	transmembrane protein induced by tumor necrosis factor alpha	TMPIT	83862	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
219368_at	nucleosome assembly protein 1-like 2	NAP1L2	4674	3
212253_x_at	dystonin	DST	667	3
230433_at	hypothetical gene supported by AK094796	LOC400764	400764	3
225978_at	family with sequence similarity 80, member B	FAM80B	57494	3
35846_at	thyroid hormone receptor, alpha (erythroblastic leukemia viral (v-erb-a) oncogene homolog, avian)	THRA	7067	3
201809_s_at	endoglin (Osler-Rendu-Weber syndrome 1)	ENG	2022	3
238592_at	PDZ and LIM domain 3	PDLIM3	27295	3
228115_at	Transcribed locus			3
220233_at	F-box protein 17	FBXO17	115290	3
213386_at	Chromosome 9 open reading frame 125	C9orf125	84302	3
216944_s_at	inositol 1,4,5-triphosphate receptor, type 1	ITPR1	3708	3
205439_at	glutathione S-transferase theta 2	GSTT2	2953	3
203796_s_at	B-cell CLL/lymphoma 7A	BCL7A	605	3
210688_s_at	carnitine palmitoyltransferase 1A (liver)	CPT1A	1374	3
223208_at	potassium channel tetramerisation domain containing 10	KCTD10	83892	3
237664_at	Protein tyrosine phosphatase-like (proline instead of catalytic arginine), member a	PTPLA	9200	3
226744_at	hypothetical protein MGC3329	MGC3329	79066	3
226313_at	chromosome 10 open reading frame 35	C10orf35	219738	3
228523_at	nanos homolog 1 (Drosophila)	NANOS1	340719	3
229876_at	Phosphorylase kinase, alpha 1 (muscle)	PHKA1	5255	3
242519_at	Selenoprotein P, plasma, 1	SEPP1	6414	3
214433_s_at	selenium binding protein 1 ; selenium binding protein 1	SELENBP1	8991	3
223237_x_at	adaptor-related protein complex 2, alpha 1 subunit	AP2A1	160	3
222834_s_at	guanine nucleotide binding protein (G protein), gamma 12	GNG12	55970	3
203019_x_at	synovial sarcoma, X breakpoint 2 interacting protein	SSX2IP	117178	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
225044_at	hypothetical protein MGC20781	MGC20781	115024	3
209047_at	aquaporin 1 (channel-forming integral protein, 28kDa)	AQP1	358	3
225868_at	tripartite motif-containing 47	TRIM47	91107	3
226168_at	zinc finger, AN1-type domain 2B	ZFAND2B	130617	3
213992_at	collagen, type IV, alpha 6	COL4A6	1288	3
205110_s_at	fibroblast growth factor 13	FGF13	2258	3
204395_s_at	G protein-coupled receptor kinase 5	GRK5	2869	3
223539_s_at	small EDRK-rich factor 1A (telomeric) ;	SERF1A	56617	3
225979_at	pleckstrin homology domain containing, family G (with RhoGef domain) member 2	PLEKHG2	64857	3
228584_at	sarcoglycan, beta (43kDa dystrophin-associated glycoprotein)	SGCB	6443	3
218094_s_at	chromosome 20 open reading frame 35	C20orf35	55861	3
204497_at	adenylate cyclase 9	ADCY9	115	3
227308_x_at	latent transforming growth factor beta binding protein 3	LTBP3	4054	3
228728_at	hypothetical protein FLJ21986	FLJ21986	79974	3
235083_at	hypothetical protein FLJ38359	FLJ38359	151009	3
205381_at	leucine rich repeat containing 17	LRRC17	10234	3
212728_at	discs, large homolog 3 (neuroendocrine-dlg, Drosophila)	DLG3	1741	3
221708_s_at	smooth muscle cell associated protein-1 ; smooth muscle cell associated protein-1	SMAP-1	55898	3
201867_s_at	transducin (beta)-like 1X-linked	TBL1X	6907	3
208827_at	proteasome (prosome, macropain) subunit, beta type, 6	PSMB6	5694	3
203919_at	transcription elongation factor A (SII), 2	TCEA2	6919	3
210790_s_at	SAR1 gene homolog A (S. cerevisiae)	SAR1A	56681	3
203033_x_at	fumarate hydratase	FH	2271	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
230287_at	RUN and TBC1 domain containing 2	RUTBC2	129049	3
201261_x_at	biglycan	BGN	633	3
225021_at	zinc finger protein 532	ZNF532	55205	3
241873_at	Unc-5 homolog C (C. elegans)	UNC5C	8633	3
202364_at	MAX interactor 1 ; MAX interactor 1	MXI1	4601	3
209885_at	ras homolog gene family, member D	RHOD	29984	3
212197_x_at	myosin phosphatase-Rho interacting protein	M-RIP	23164	3
203410_at	adaptor-related protein complex 3, mu 2 subunit	AP3M2	10947	3
214318_s_at	hypothetical protein CG003	13CDNA73	10129	3
212647_at	related RAS viral (r-ras) oncogene homolog	RRAS	6237	3
224624_at	leucine rich repeat containing 8 family, member A	LRRC8A	56262	3
212566_at	microtubule-associated protein 4	MAP4	4134	3
1558348_at	De-etiolated homolog 1 (Arabidopsis)	DET1	55070	3
221527_s_at	par-3 partitioning defective 3 homolog (C. elegans)	PARD3	56288	3
210519_s_at	NAD(P)H dehydrogenase, quinone 1	NQO1	1728	3
209292_at	Inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	ID4	3400	3
238204_at	Leiomodin 1 (smooth muscle)	LMOD1	25802	3
1569150_x_at	PDZ and LIM domain 7 (enigma)	PDLIM7	9260	3
244370_at	KIAA2022 protein	KIAA2022	340533	3
228278_at	nuclear factor I/X (CCAAT-binding transcription factor)	NFIX	4784	3
227166_at	DnaJ (Hsp40) homolog, subfamily C, member 18	DNAJC18	202052	3
207839_s_at	chromosome 9 open reading frame 127	C9orf127	51754	3
1552520_at	transmembrane protein 74	TMEM74	157753	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
209191_at	tubulin, beta 6	TUBB6	84617	3
238477_at	Kinesin family member 1C	KIF1C	10749	3
219468_s_at	CUE domain containing 1	CUEDC1	404093	3
204248_at	guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	3
206511_s_at	sine oculis homeobox homolog 2 (Drosophila)	SIX2	10736	3
1556325_at	filamin A interacting protein 1	FILIP1	27145	3
227705_at	transcription elongation factor A (SII)-like 7	TCEAL7	56849	3
1557458_s_at	Src homology 2 domain containing adaptor protein B	SHB	6461	3
1555390_at	chromosome 14 open reading frame 21	C14orf21	161424	3
1554614_a_at	polypyrimidine tract binding protein 2	PTBP2	58155	3
227545_at	BRCA1 associated RING domain 1	BARD1	580	3
233540_s_at	CDK5 regulatory subunit associated protein 2	CDK5RAP2	55755	3
232027_at	spectrin repeat containing, nuclear envelope 1	SYNE1	23345	3
212599_at	autism susceptibility candidate 2	AUTS2	26053	3
205398_s_at	SMAD, mothers against DPP homolog 3 (Drosophila)	SMAD3	4088	3
230630_at	Adenylate kinase 3-like 1	AK3	205	3
212494_at	tensin like C1 domain containing phosphatase (tensin 2)	TENC1	23371	3
211564_s_at	PDZ and LIM domain 4	PDLIM4	8572	3
211003_x_at	transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)	TGM2	7052	3
236234_at	phosphodiesterase 1A, calmodulin-dependent	PDE1A	5136	3
203263_s_at	Cdc42 guanine nucleotide exchange factor (GEF) 9	ARHGEF9	23229	3
225693_s_at	calmodulin binding transcription activator 1	CAMTA1	23261	3
204984_at	glypican 4	GPC4	2239	3
213467_at	Rho family GTPase 2	RND2	8153	3
224710_at	RAB34, member RAS oncogene family	RAB34	83871	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
212895_s_at	active BCR-related gene	ABR	29	3
224720_at	mindbomb homolog 1 (Drosophila)	MIB1	57534	3
213578_at	bone morphogenetic protein receptor, type IA	BMPR1A	657	3
208848_at	alcohol dehydrogenase 5 (class III), chi polypeptide	ADH5	128	3
207747_s_at	docking protein 4	DOK4	55715	3
212673_at	methionyl aminopeptidase 1	METAP1	23173	3
220935_s_at	CDK5 regulatory subunit associated protein 2	CDK5RAP2	55755	3
228292_at	Glucosidase, beta (bile acid) 2	GBA2	57704	3
1564002_a_at	chromosome 6 open reading frame 199	C6orf199	221264	3
204686_at	insulin receptor substrate 1	IRS1	3667	3
218180_s_at	EPS8-like 2	EPS8L2	64787	3
221207_s_at	neurobeachin	NBEA	26960	3
202089_s_at	solute carrier family 39 (zinc transporter), member 6	SLC39A6	25800	3
205543_at	heat shock 70kDa protein 4-like	HSPA4L	22824	3
201267_s_at	proteasome (prosome, macropain) 26S subunit, ATPase, 3	PSMC3	5702	3
1556047_s_at	melanoma antigen family E, 1	MAGEE1	57692	3
204281_at	TEA domain family member 4	TEAD4	7004	3
213400_s_at	transducin (beta)-like 1X-linked	TBL1X	6907	3
201161_s_at	cold shock domain protein A	CSDA	8531	3
201042_at	transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)	TGM2	7052	3
212983_at	v-Ha-ras Harvey rat sarcoma viral oncogene homolog	HRAS	3265	3
219610_at	Rho-guanine nucleotide exchange factor	RGNEF	64283	3
203264_s_at	Cdc42 guanine nucleotide exchange factor (GEF) 9	ARHGEF9	23229	3
225104_at	zinc finger protein 598	ZNF598	90850	3
40562_at	guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
209210_s_at	pleckstrin homology domain containing, family C (with FERM domain) member 1	PLEKHC1	10979	3
213476_x_at	tubulin, beta 3	TUBB3	10381	3
225677_at	B-cell receptor-associated protein 29	BCAP29	55973	3
1559388_a_at	Ly6/neurotoxin 1	LYNX1	66004	3
212439_at	inositol hexaphosphate kinase 1	IHPK1	9807	3
210870_s_at	epilepsy, progressive myoclonus type 2A, Lafora disease (laforin)	EPM2A	7957	3
228233_at	FRAS1 related extracellular matrix 1	FREM1	158326	3
202218_s_at	fatty acid desaturase 2	FADS2	9415	3
226869_at	EGF-like-domain, multiple 3	EGFL3	1953	3
224445_s_at	zinc finger, FYVE domain containing 21 ; zinc finger, FYVE domain containing 21	ZFYVE21	79038	3
1569796_s_at	attractin-like 1	ATRNL1	26033	3
225915_at	calcium binding protein 39-like	CAB39L	81617	3
223019_at	chromosome 9 open reading frame 88	C9orf88	64855	3
202694_at	serine/threonine kinase 17a (apoptosis-inducing)	STK17A	9263	3
225665_at	sterile alpha motif and leucine zipper containing kinase AZK	ZAK	51776	3
225105_at	hypothetical protein	LOC387882	387882	3
239342_at	diacylglycerol kinase, zeta 104kDa	DGKZ	8525	3
223316_at	coiled-coil domain containing 3	CCDC3	83643	3
215537_x_at	dimethylarginine dimethylaminohydrolase 2	DDAH2	23564	3
1569208_a_at	KIAA1102 protein	KIAA1102	22998	3
236634_at	chromosome 8 open reading frame 48	C8orf48	157773	3
217657_at	B-cell receptor-associated protein 29	BCAP29	55973	3
223593_at	aminoadipate aminotransferase	AADAT	51166	3
212828_at	synaptojanin 2	SYNJ2	8871	3
225662_at	sterile alpha motif and leucine zipper containing kinase AZK	ZAK	51776	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
227862_at	hypothetical LOC388610	LOC388610	388610	3
208677_s_at	basigin (OK blood group)	BSG	682	3
218612_s_at	tumor suppressing subtransferable candidate 4	TSSC4	10078	3
201714_at	tubulin, gamma 1	TUBG1	7283	3
203627_at	Insulin-like growth factor 1 receptor	IGF1R	3480	3
227846_at	putative G protein coupled receptor	GPR	11245	3
201802_at	solute carrier family 29 (nucleoside transporters), member 1	SLC29A1	2030	3
222559_s_at	hypothetical protein FLJ10656	P15RS	55197	3
1555630_a_at	RAB34, member RAS oncogene family	RAB34	83871	3
202111_at	solute carrier family 4, anion exchanger, member 2 (erythrocyte membrane protein band 3-like 1)	SLC4A2	6522	3
204347_at	adenylate kinase 3-like 1 ; adenylate kinase 3-like 2	AK3L1	205 ; 387851	3
228355_s_at	Myc-induced mitochondria protein	mimitin	91942	3
226933_s_at	Inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	ID4	3400	3
227944_at	protein tyrosine phosphatase, non-receptor type 3	PTPN3	5774	3
213079_at	hypothetical protein DT1P1A10	RP1-112K5.2	90121	3
224984_at	nuclear factor of activated T-cells 5, tonicity-responsive	NFAT5	10725	3
222998_at	MAF1 homolog (S. cerevisiae)	MAF1	84232	3
225288_at	Collagen, type XXVII, alpha 1	COL27A1	85301	3
219304_s_at	platelet derived growth factor D	PDGFD	80310	3
200840_at	lysyl-tRNA synthetase	KARS	3735	3
212703_at	talin 2	TLN2	83660	3
202344_at	heat shock transcription factor 1	HSF1	3297	3
214823_at	zinc finger protein 204	ZNF204	7754	3
209311_at	BCL2-like 2	BCL2L2	599	3
214073_at	cortactin	CTTN	2017	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
212736_at	chromosome 16 open reading frame 45	C16orf45	89927	3
204688_at	sarcoglycan, epsilon	SGCE	8910	3
218651_s_at	La ribonucleoprotein domain family, member 6	LARP6	55323	3
228548_at	RAP1A, member of RAS oncogene family	RAP1A	5906	3
230309_at	Betaine-homocysteine methyltransferase 2	BHMT2	23743	3
205740_s_at	hypothetical protein MGC10433	MGC10433	79171	3
1554004_a_at	Rho-guanine nucleotide exchange factor	RGNEF	64283	3
212525_s_at	H2A histone family, member X	H2AFX	3014	3
218634_at	pleckstrin homology-like domain, family A, member 3	PHLDA3	23612	3
226705_at	Fibroblast growth factor receptor 1 (fms-related tyrosine kinase 2, Pfeiffer syndrome)	FGFR1	2260	3
227543_at	HIV-1 Tat interacting protein, 60kDa	HTATIP	10524	3
218823_s_at	potassium channel tetramerisation domain containing 9	KCTD9	54793	3
225806_at	jub, ajuba homolog (Xenopus laevis)	JUB	84962	3
229286_at	melanoma antigen family E, 1	MAGEE1	57692	3
211043_s_at	clathrin, light polypeptide (Lcb) ; clathrin, light polypeptide (Lcb)	CLTB	1212	3
244246_at	mirror-image polydactyly 1	MIPOL1	145282	3
224397_s_at	ARG99 protein ; ARG99 protein	ARG99	83857	3
206037_at	cysteine conjugate-beta lyase; cytoplasmic (glutamine transaminase K, kyneurenine aminotransferase)	CCBL1	883	3
212914_at	chromobox homolog 7	CBX7	23492	3
213726_x_at	tubulin, beta, 2	TUBB2	10383	3
212510_at	glycerol-3-phosphate dehydrogenase 1-like	GPD1L	23171	3
222582_at	protein kinase, AMP-activated, gamma 2 non-catalytic subunit	PRKAG2	51422	3
203835_at	leucine rich repeat containing 32	LRRC32	2615	3
213977_s_at	CDKN1A interacting zinc finger protein 1	CIZ1	25792	3
217359_s_at	neural cell adhesion molecule 1	NCAM1	4684	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
226710_at	similar to RIKEN cDNA C030006K11 gene	MGC70857	414919	3
225308_s_at	TPR domain, ankyrin-repeat and coiled-coil-containing	TANC	85461	3
201231_s_at	enolase 1, (alpha)	ENO1	2023	3
1554008_at	oncostatin M receptor	OSMR	9180	3
224365_s_at	tigger transposable element derived 7 ; tigger transposable element derived 7	TIGD7	91151	3
202755_s_at	glypican 1	GPC1	2817	3
203450_at	PKD2 interactor, golgi and endoplasmic reticulum associated 1	PGEA1	25776	3
221016_s_at	transcription factor 7-like 1 (T-cell specific, HMG-box)	TCF7L1	83439	3
215735_s_at	tuberous sclerosis 2	TSC2	7249	3
243502_at	Gap junction protein, alpha 7, 45kDa (connexin 45)	GJA7	10052	3
221216_s_at	sex comb on midleg homolog 1 (Drosophila)	SCMH1	22955	3
209156_s_at	collagen, type VI, alpha 2	COL6A2	1292	3
222778_s_at	Wolf-Hirschhorn syndrome candidate 1	WHSC1	7468	3
227572_at	Ubiquitin specific peptidase 30	USP30	84749	3
216836_s_at	v-erb-b2 erythroblastic leukemia viral oncogene homolog 2	ERBB2	2064	3
223576_at	chromosome 6 open reading frame 203	C6orf203	51250	3
213424_at	KIAA0895 protein	KIAA0895	23366	3
241963_at	zinc finger protein 704	ZNF704	619279	3
201027_s_at	eukaryotic translation initiation factor 5B	EIF5B	9669	3
228104_at	plexin A4, A	PLXNA4A	57671	3
212135_s_at	ATPase, Ca++ transporting, plasma membrane 4	ATP2B4	493	3
1553764_a_at	jub, ajuba homolog (Xenopus laevis)	JUB	84962	3
220032_at	hypothetical protein FLJ21986	FLJ21986	79974	3
200659_s_at	prohibitin	PHB	5245	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
202616_s_at	methyl CpG binding protein 2 (Rett syndrome)	MECP2	4204	3
218373_at	fused toes homolog (mouse)	FTS	64400	3
201373_at	plectin 1, intermediate filament binding protein 500kDa	PLEC1	5339	3
218762_at	zinc finger protein 574	ZNF574	64763	3
223805_at	oxysterol binding protein-like 6	OSBPL6	114880	3
232051_at	hypothetical protein LOC92922	MGC10992	92922	3
234734_s_at	trinucleotide repeat containing 6A	TNRC6A	27327	3
242590_at	RNA (guanine-9-) methyltransferase domain containing 3	RG9MTD3	158234	3
204904_at	gap junction protein, alpha 4, 37kDa (connexin 37)	GJA4	2701	3
225450_at	angiomotin like 1	AMOTL1	154810	3
205824_at	heat shock 27kDa protein 2	HSPB2	3316	3
44702_at	synapse defective 1, Rho GTPase, homolog 1 (C. elegans)	SYDE1	85360	3
224999_at	Epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	EGFR	1956	3
229507_at	similar to RIKEN cDNA 6530418L21	LOC389119	389119	3
222668_at	potassium channel tetramerisation domain containing 15	KCTD15	79047	3
201430_s_at	dihydropyrimidinase-like 3	DPYSL3	1809	3
222760_at	zinc finger protein 703	ZNF703	80139	3
201035_s_at	L-3-hydroxyacyl-Coenzyme A dehydrogenase, short chain	HADHSC	3033	3
232983_s_at	deafness locus associated putative guanine nucleotide exchange factor	DELGEF	26297	3
205712_at	protein tyrosine phosphatase, receptor type, D	PTPRD	5789	3
227219_x_at	microtubule-associated protein 1 light chain 3 alpha	MAP1LC3A	84557	3
244057_s_at	chromosome 10 open reading frame 72	C10orf72	196740	3
232282_at	WNK lysine deficient protein kinase 3	WNK3	65267	3
213066_at	RUN and SH3 domain containing 2	RUSC2	9853	3
206698_at	Kell blood group precursor (McLeod phenotype)	XK	7504	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
210751_s_at	regucalcin (senescence marker protein-30)	RGN	9104	3
229257_at	KIAA1856 protein	KIAA1856	84629	3
222489_s_at	Werner helicase interacting protein 1	WRNIP1	56897	3
209432_s_at	cAMP responsive element binding protein 3	CREB3	10488	3
212081_x_at	HLA-B associated transcript 2	BAT2	7916	3
228370_at	Small nuclear ribonucleoprotein polypeptide N	SNRPN	6638	3
235109_at	Zinc finger, BED-type containing 3	ZBED3	84327	3
202468_s_at	catenin (cadherin-associated protein), alpha-like 1	CTNNAL1	8727	3
202316_x_at	ubiquitination factor E4B (UFD2 homolog, yeast)	UBE4B	10277	3
213887_s_at	polymerase (RNA) II (DNA directed) polypeptide E, 25kDa	POLR2E	5434	3
212045_at	golgi apparatus protein 1	GLG1	2734	3
212776_s_at	obscurin-like 1	OBSL1	23363	3
225923_at	VAMP (vesicle-associated membrane protein)-associated protein B and C	VAPB	9217	3
207842_s_at	cancer susceptibility candidate 3	CASC3	22794	3
242828_at	Fidgetin	FIGN	55137	3
200764_s_at	catenin (cadherin-associated protein), alpha 1, 102kDa	CTNNA1	1495	3
205726_at	diaphanous homolog 2 (Drosophila)	DIAPH2	1730	3
205158_at	ribonuclease, RNase A family, 4	RNASE4	6038	3
215210_s_at	dihydrolipoamide S-succinyltransferase (E2 component of 2-oxo-glutarate complex)	DLST ; DLSTP	1743 ; 1744	3
233825_s_at	CD99 antigen-like 2	CD99L2	83692	3
41037_at	TEA domain family member 4	TEAD4	7004	3
240063_at	hypothetical LOC 441046	LOC441046	441046	3
217607_x_at	eukaryotic translation initiation factor 4 gamma, 2	EIF4G2	1982	3
202801_at	protein kinase, cAMP-dependent, catalytic, alpha	PRKACA	5566	3
212343_at	Yip1 domain family, member 6	YIPF6	286451	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201039_s_at	RAD23 homolog A (S. cerevisiae)	RAD23A	5886	3
225018_at	spire homolog 1 (Drosophila)	SPIRE1	56907	3
218686_s_at	rhomboid family 1 (Drosophila)	RHBDF1	64285	3
213905_x_at	biglycan ; serologically defined colon cancer antigen 33	BGN	10194 ; 633	3
203896_s_at	phospholipase C, beta 4	PLCB4	5332	3
207808_s_at	protein S (alpha)	PROS1	5627	3
219104_at	ring finger protein 141	RNF141	50862	3
225871_at	six transmembrane epithelial antigen of the prostate 2	STEAP2	261729	3
211737_x_at	pleiotrophin (heparin binding growth factor 8, neurite growth-promoting factor 1)	PTN	5764	3
220200_s_at	PR/SET domain containing protein 8	SET8	387893	3
241897_at	RNA binding protein with multiple splicing	RBPMS	11030	3
219298_at	enoyl Coenzyme A hydratase domain containing 3	ECHDC3	79746	3
226581_at	zinc finger, FYVE domain containing 20	ZFYVE20	64145	3
236657_at	Full length insert cDNA YI37C01			3
203895_at	phospholipase C, beta 4	PLCB4	5332	3
222240_s_at	myo-inositol 1-phosphate synthase A1	ISYNA1	51477	3
209099_x_at	jagged 1 (Alagille syndrome)	JAG1	182	3
235467_s_at	potassium voltage-gated channel, Shaw-related subfamily, member 4	KCNC4	3749	3
228224_at	proline/arginine-rich end leucine-rich repeat protein	PRELP	5549	3
208831_x_at	suppressor of Ty 6 homolog (S. cerevisiae)	SUPT6H	6830	3
217918_at	dynein, cytoplasmic, light polypeptide 2A	DNCL2A	83658	3
215407_s_at	astrotactin 2	ASTN2	23245	3
225745_at	low density lipoprotein receptor-related protein 6	LRP6	4040	3
212484_at	family with sequence similarity 89, member B	FAM89B	23625	3
212350_at	TBC1 (tre-2/USP6, BUB2, cdc16) domain family, member 1	TBC1D1	23216	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
209291_at	inhibitor of DNA binding 4, dominant negative helix-loop-helix protein	ID4	3400	3
205932_s_at	msh homeo box homolog 1 (Drosophila)	MSX1	4487	3
223353_at	HCCA2 protein	HCCA2	81532	3
213343_s_at	glycerophosphodiester phosphodiesterase domain containing 5	GDPD5	81544	3
212958_x_at	peptidylglycine alpha-amidating monooxygenase	PAM	5066	3
226638_at	Rho GTPase activating protein 23	ARHGAP23	57636	3
236565_s_at	La ribonucleoprotein domain family, member 6	LARP6	55323	3
221567_at	nucleolar protein 3 (apoptosis repressor with CARD domain)	NOL3	8996	3
228930_at	Hypothetical protein LOC123722	LOC123722	123722	3
235977_at	MRNA; cDNA DKFZp686N1345 (from clone DKFZp686N1345)			3
236656_s_at	Full length insert cDNA YI37C01			3
201194_at	selenoprotein W, 1	SEPW1	6415	3
238322_s_at	TEA domain family member 2	TEAD2	8463	3
204447_at	ProSAPiP1 protein	ProSAPiP1	9762	3
218425_at	TRIAD3 protein	TRIAD3	54476	3
209197_at	synaptotagmin XI	SYT11	23208	3
218110_at	XPA binding protein 2	XAB2	56949	3
1569512_at	Supervillin	SVIL	6840	3
200697_at	hexokinase 1	HK1	3098	3
202154_x_at	tubulin, beta 3	TUBB3	10381	3
238426_at	hypothetical protein DKFZp761L1417	DKFZp761L1417	222865	3
205280_at	glycine receptor, beta	GLRB	2743	3
1555724_s_at	transgelin	TAGLN	6876	3
232224_at	mannan-binding lectin serine peptidase 1 (C4/C2 activating component of Ra-reactive factor)	MASP1	5648	3
200765_x_at	catenin (cadherin-associated protein), alpha 1, 102kDa	CTNNA1	1495	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
214771_x_at	myosin phosphatase-Rho interacting protein	M-RIP	23164	3
212243_at	glutamate receptor, ionotropic, N-methyl D-aspartate-like 1A ; GRINL1A combined protein	GRINL1A	145781	3
215230_x_at	eukaryotic translation initiation factor 3, subunit 8, 110kDa	EIF3S8	8663	3
214656_x_at	myosin IC	MYO1C	4641	3
212503_s_at	KIAA0934	KIAA0934	22982	3
216215_s_at	RNA binding motif protein 9	RBM9	23543	3
226683_at	Sorting nexin associated golgi protein 1	SNAG1	112574	3
232322_x_at	START domain containing 10	STARD10	10809	3
212727_at	discs, large homolog 3 (neuroendocrine-dlg, Drosophila)	DLG3	1741	3
228563_at	gap junction protein, alpha 7, 45kDa (connexin 45)	GJA7	10052	3
220748_s_at	zinc finger protein 580	ZNF580	51157	3
202245_at	lanosterol synthase (2,3-oxidosqualene-lanosterol cyclase)	LSS	4047	3
213942_at	EGF-like-domain, multiple 3	EGFL3	1953	3
205121_at	sarcoglycan, beta (43kDa dystrophin-associated glycoprotein)	SGCB	6443	3
1554597_at	hypothetical gene supported by AK092922; AL831912	LOC440426	440426	3
219251_s_at	WD repeat domain 60	WDR60	55112	3
222217_s_at	solute carrier family 27 (fatty acid transporter), member 3	SLC27A3	11000	3
201328_at	v-ets erythroblastosis virus E26 oncogene homolog 2 (avian)	ETS2	2114	3
203068_at	kelch-like 21 (Drosophila)	KLHL21	9903	3
211275_s_at	glycogenin	GYG	2992	3
228639_at	FYVE, RhoGEF and PH domain containing 1 (faciogenital dysplasia)	FGD1	2245	3
1552670_a_at	hypothetical protein LOC286044	LOC286044	286044	3
201115_at	polymerase (DNA directed), delta 2, regulatory subunit 50kDa	POLD2	5425	3
219431_at	Rho GTPase activating protein 10	ARHGAP10	79658	3
214724_at	DIX domain containing 1	DIXDC1	85458	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
209394_at	acetylserotonin O-methyltransferase-like	ASMTL	8623	3
228027_at	G protein-coupled receptor associated sorting protein 2	GPRASP2	114928	3
215329_s_at	cell division cycle 2-like 1 (PITSLRE proteins)	CDC2L1	984	3
201313_at	enolase 2 (gamma, neuronal)	ENO2	2026	3
226647_at	transmembrane protein 25	TMEM25	84866	3
231430_at	hypothetical protein MGC33846	MGC33846	220382	3
225080_at	Myosin IC	MYO1C	4641	3
225704_at	KIAA1545 protein	KIAA1545	57666	3
218695_at	exosome component 4	EXOSC4	54512	3
242731_x_at	Transcribed locus			3
200619_at	splicing factor 3b, subunit 2, 145kDa	SF3B2	10992	3
225674_at	B-cell receptor-associated protein 29	BCAP29	55973	3
223005_s_at	chromosome 9 open reading frame 5	C9orf5	23731	3
216028_at	DKFZP564C152 protein	DKFZP564C152	26120	3
217561_at	calcitonin/calcitonin-related polypeptide, alpha	CALCA	796	3
235541_at	LAS1-like (S. cerevisiae)	LAS1L	81887	3
210987_x_at	tropomyosin 1 (alpha)	TPM1	7168	3
228456_s_at	hypothetical protein LOC149832	LOC149832	149832	3
219039_at	block of proliferation 1	BOP1	23246	3
228461_at	SH3 multiple domains 4	SH3MD4	344558	3
243111_at	Weakly similar to zinc finger protein 195	FLJ34077	404033	3
219379_x_at	zinc finger protein 358	ZNF358	140467	3
212807_s_at	sortilin 1	SORT1	6272	3
230750_at	RAB23, member RAS oncogene family	RAB23	51715	3
217943_s_at	arginine/proline rich coiled-coil 1	RPRC1	55700	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
219863_at	hect domain and RLD 5	HERC5	51191	3
233919_s_at	hyaluronan binding protein 4	HABP4	22927	3
207163_s_at	v-akt murine thymoma viral oncogene homolog 1	AKT1	207	3
214078_at	P21 (CDKN1A)-activated kinase 3	PAK3	5063	3
227882_at	fukutin related protein	FKRP	79147	3
219087_at	asporin (LRR class 1)	ASPN	54829	3
225016_at	adenomatosis polyposis coli down-regulated 1	APCDD1	147495	3
207169_x_at	discoidin domain receptor family, member 1	DDR1	780	3
1552735_at	protocadherin gamma subfamily A, 4	PCDHGA4	56111	3
209213_at	carbonyl reductase 1	CBR1	873	3
202455_at	histone deacetylase 5	HDAC5	10014	3
218175_at	limkain beta 2	FLJ22471	80212	3
225303_at	kin of IRRE like (Drosophila)	KIRREL	55243	3
201036_s_at	L-3-hydroxyacyl-Coenzyme A dehydrogenase, short chain	HADHSC	3033	3
204223_at	proline/arginine-rich end leucine-rich repeat protein	PRELP	5549	3
217196_s_at	calmodulin regulated spectrin-associated protein 1-like 1	CAMSAP1L1	23271	3
223007_s_at	chromosome 9 open reading frame 5	C9orf5	23731	3
238636_at	hypothetical protein LOC283439	LOC283439	283439	3
226895_at	Nuclear factor I/C (CCAAT-binding transcription factor)	NFIC	4782	3
217911_s_at	BCL2-associated athanogene 3	BAG3	9531	3
1560359_at	Pelota homolog (Drosophila)	PELO	53918	3
222221_x_at	EH-domain containing 1	EHD1	10938	3
212747_at	ankyrin repeat and sterile alpha motif domain containing 1	ANKS1	23294	3
204001_at	small nuclear RNA activating complex, polypeptide 3, 50kDa	SNAPC3	6619	3
217427_s_at	HIR histone cell cycle regulation defective homolog A (S. cerevisiae)	HIRA	7290	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201830_s_at	neuroepithelial cell transforming gene 1	NET1	10276	3
225963_at	kelch domain containing 5	KLHDC5	57542	3
201537_s_at	dual specificity phosphatase 3 (vaccinia virus phosphatase VH1-related)	DUSP3	1845	3
226655_at	Syntaxin 17	STX17	55014	3
233563_s_at	cleavage and polyadenylation specific factor 3-like	CPSF3L	54973	3
227029_at	chromosome 14 open reading frame 24	C14orf24	283635	3
1553646_at	chromosome X open reading frame 43	CXorf43	139324	3
209693_at	astrotactin 2	ASTN2	23245	3
212741_at	monoamine oxidase A	MAOA	4128	3
211714_x_at	tubulin, beta polypeptide ; tubulin, beta polypeptide	TUBB	203068	3
216271_x_at	synapse defective 1, Rho GTPase, homolog 1 (C. elegans)	SYDE1	85360	3
204716_at	coiled-coil domain containing 6	CCDC6	8030	3
204993_at	guanine nucleotide binding protein (G protein), alpha z polypeptide	GNAZ	2781	3
203894_at	tubulin, gamma 2	TUBG2	27175	3
1560648_s_at	TSPY-like 1	TSPYL1	7259	3
219440_at	retinoic acid induced 2	RAI2	10742	3
226846_at	phytanoyl-CoA dioxygenase domain containing 1	PHYHD1	254295	3
226938_at	WD repeat domain 21A	WDR21A	26094	3
214671_s_at	active BCR-related gene	ABR	29	3
226231_at	PRKC, apoptosis, WT1, regulator	PAWR	5074	3
226718_at	adhesion molecule with Ig-like domain 1	AMIGO1	57463	3
210882_s_at	trophinin	TRO	7216	3
214743_at	cut-like 1, CCAAT displacement protein (Drosophila)	CUTL1	1523	3
208703_s_at	amyloid beta (A4) precursor-like protein 2	APLP2	334	3
225315_at	mitochondrial ribosomal protein L21	MRPL21	219927	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
212813_at	junctional adhesion molecule 3	JAM3	83700	3
201829_at	neuroepithelial cell transforming gene 1	NET1	10276	3
238613_at	sterile alpha motif and leucine zipper containing kinase AZK	ZAK	51776	3
208636_at	Actinin, alpha 1	ACTN1	87	3
224281_s_at	neugrin, neurite outgrowth associated	NGRN	51335	3
222558_at	hypothetical protein FLJ10656	P15RS	55197	3
208723_at	ubiquitin specific peptidase 11	USP11	8237	3
209361_s_at	poly(rC) binding protein 4	PCBP4	57060	3
204834_at	fibrinogen-like 2	FGL2	10875	3
204005_s_at	PRKC, apoptosis, WT1, regulator	PAWR	5074	3
227688_at	leucine-rich repeats and calponin homology (CH) domain containing 2	LRCH2	57631	3
225650_at	sterile alpha motif domain containing 1	SAMD1	90378	3
214909_s_at	dimethylarginine dimethylaminohydrolase 2	DDAH2	23564	3
204682_at	latent transforming growth factor beta binding protein 2	LTBP2	4053	3
229884_s_at	mitochondrial ribosomal protein L2	MRPL2	51069	3
218813_s_at	SH3-domain GRB2-like endophilin B2	SH3GLB2	56904	3
235295_at	Pannexin 1	PANX1	24145	3
208789_at	polymerase I and transcript release factor	PTRF	284119	3
241442_at	Dishevelled associated activator of morphogenesis 2	DAAM2	23500	3
210871_x_at	synovial sarcoma, X breakpoint 2 interacting protein	SSX2IP	117178	3
228255_at	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 4	ALS2CR4	65062	3
226451_at	similar to RIKEN cDNA B230118G17 gene	MGC19604	112812	3
204344_s_at	Sec23 homolog A (S. cerevisiae)	SEC23A	10484	3
228520_s_at	Amyloid beta (A4) precursor-like protein 2	APLP2	334	3
213298_at	nuclear factor I/C (CCAAT-binding transcription factor)	NFIC	4782	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
218029_at	family with sequence similarity 65, member A	FAM65A	79567	3
231137_at	Acyl-CoA synthetase bubblegum family member 1	BG1	23205	3
1553204_at	hypothetical protein FLJ30313	FLJ30313	253868	3
202196_s_at	dickkopf homolog 3 (Xenopus laevis)	DKK3	27122	3
213336_at	Bromodomain adjacent to zinc finger domain, 1B	BAZ1B	9031	3
212294_at	guanine nucleotide binding protein (G protein), gamma 12	GNG12	55970	3
223116_at	breast cancer anti-estrogen resistance 1	BCAR1	9564	3
205657_at	3-hydroxyanthranilate 3,4-dioxygenase	HAAO	23498	3
203686_at	N-methylpurine-DNA glycosylase	MPG	4350	3
1552708_a_at	dual specificity phosphatase 19	DUSP19	142679	3
222469_s_at	toll interacting protein	TOLLIP	54472	3
242137_at	RNA binding motif, single stranded interacting protein	RBMS3	27303	3
222463_s_at	beta-site APP-cleaving enzyme 1	BACE1	23621	3
209242_at	paternally expressed 3	PEG3	5178	3
37462_i_at	splicing factor 3a, subunit 2, 66kDa	SF3A2	8175	3
209614_at	alcohol dehydrogenase 1A (class I), alpha polypeptide	ADH1A	124	3
202249_s_at	WD repeat domain 42A	WDR42A	50717	3
229991_s_at	Synaptotagmin-like 4 (granuphilin-a)	SYTL4	94121	3
205273_s_at	pitrilysin metallopeptidase 1	PITRM1	10531	3
204106_at	testis-specific kinase 1	TESK1	7016	3
217286_s_at	NDRG family member 3	NDRG3	57446	3
226587_at	Small nuclear ribonucleoprotein polypeptide N	SNRPN	6638	3
209198_s_at	synaptotagmin XI	SYT11	23208	3
218590_at	progressive external ophthalmoplegia 1	PEO1	56652	3
202440_s_at	suppression of tumorigenicity 5	ST5	6764	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
230369_at	G protein-coupled receptor 161	GPR161	23432	3
212851_at	DCN1, defective in cullin neddylation 1, domain containing 4 (S. cerevisiae)	DCUN1D4	23142	3
205354_at	guanidinoacetate N-methyltransferase	GAMT	2593	3
1560296_at	Dystonin	DST	667	3
202762_at	Rho-associated, coiled-coil containing protein kinase 2	ROCK2	9475	3
223152_at	protein phosphatase 1, regulatory (inhibitor) subunit 12C	PPP1R12C	54776	3
219180_s_at	peroxisome biogenesis factor 26	PEX26	55670	3
212674_s_at	DEAH (Asp-Glu-Ala-His) box polypeptide 30	DHX30	22907	3
222887_s_at	hypothetical protein FLJ20507	FLJ20507	55654	3
242738_s_at	AT-binding transcription factor 1	ATBF1	463	3
231157_at	tubulin tyrosine ligase-like family, member 11	TTLL11	158135	3
208740_at	sin3-associated polypeptide, 18kDa	SAP18	10284	3
202275_at	glucose-6-phosphate dehydrogenase	G6PD	2539	3
41657_at	serine/threonine kinase 11 (Peutz-Jeghers syndrome)	STK11	6794	3
217773_s_at	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 4, 9kDa	NDUFA4	4697	3
201961_s_at	ring finger protein 41	RNF41	10193	3
219027_s_at	myosin IXA	MYO9A	4649	3
223764_x_at	nipsnap homolog 3B (C. elegans)	NIPSNAP3B	55335	3
201082_s_at	dynactin 1 (p150, glued homolog, Drosophila)	DCTN1	1639	3
229106_at	dynein light chain 2	Dlc2	140735	3
235570_at	RNA binding motif, single stranded interacting protein	RBMS3	27303	3
223672_at	SH3-domain GRB2-like (endophilin) interacting protein 1	SGIP1	84251	3
217925_s_at	chromosome 6 open reading frame 106	C6orf106	64771	3
227325_at	hypothetical protein LOC255783	LOC255783	255783	3
212259_s_at	pre-B-cell leukemia transcription factor interacting protein 1	PBXIP1	57326	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201655_s_at	heparan sulfate proteoglycan 2 (perlecan)	HSPG2	3339	3
203906_at	IQ motif and Sec7 domain 1	IQSEC1	9922	3
214890_s_at	DKFZP564J102 protein	DKFZP564J102	25854	3
231001_at	similar to RIKEN cDNA 1110018M03	LOC387758	387758	3
224975_at	nuclear factor I/A	NFIA	4774	3
204983_s_at	glypican 4	GPC4	2239	3
1555140_a_at	BCL2-like 2	BCL2L2	599	3
217730_at	transmembrane BAX inhibitor motif containing 1	TMBIM1	64114	3
204656_at	Src homology 2 domain containing adaptor protein B	SHB	6461	3
212115_at	chromosome 16 open reading frame 34	C16orf34	90861	3
209691_s_at	docking protein 4	DOK4	55715	3
227138_at	cartilage associated protein	CRTAP	10491	3
235471_at	Chromosome 10 open reading frame 72	C10orf72	196740	3
205426_s_at	huntingtin interacting protein 1	HIP1	3092	3
223468_s_at	RGM domain family, member A	RGMA	56963	3
233720_at	Sorbin and SH3 domain containing 2	ARGBP2	8470	3
203212_s_at	myotubularin related protein 2	MTMR2	8898	3
232506_s_at	hypothetical protein HH114	HH114	84529	3
224280_s_at	family with sequence similarity 54, member B	FAM54B	56181	3
202652_at	amyloid beta (A4) precursor protein-binding, family B, member 1 (Fe65)	APBB1	322	3
63305_at	PBX/knotted 1 homeobox 2	PKNOX2	63876	3
222494_at	checkpoint suppressor 1	CHES1	1112	3
209026_x_at	tubulin, beta polypeptide	TUBB	203068	3
214940_s_at	chromosome 17 open reading frame 31	C17orf31	23293	3
226260_x_at	zinc finger protein 358	ZNF358	140467	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
227896_at	BRCA2 and CDKN1A interacting protein	BCCIP	56647	3
1553530_a_at	integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	ITGB1	3688	3
206042_x_at	small nuclear ribonucleoprotein polypeptide N ; SNRPN upstream reading frame	SNRPN	6638	3
210125_s_at	barrier to autointegration factor 1	BANF1	8815	3
213290_at	collagen, type VI, alpha 2	COL6A2	1292	3
219278_at	mitogen-activated protein kinase kinase kinase 6	MAP3K6	9064	3
224962_at	hypothetical gene supported by AK023162	LOC90120	90120	3
222016_s_at	zinc finger protein 323	ZNF323	64288	3
210958_s_at	microtubule associated serine/threonine kinase family member 4	MAST4	23227	3
212254_s_at	dystonin	DST	667	3
213488_at	sushi, nidogen and EGF-like domains 1	SNED1	25992	3
235746_s_at	phospholipase A2 receptor 1, 180kDa	PLA2R1	22925	3
204854_at	leprecan-like 2	LEPREL2	10536	3
221643_s_at	arginine-glutamic acid dipeptide (RE) repeats	RERE	473	3
211658_at	peroxiredoxin 2 ; peroxiredoxin 2	PRDX2	7001	3
217796_s_at	nuclear protein localization 4	NPL4	55666	3
209653_at	karyopherin alpha 4 (importin alpha 3)	KPNA4	3840	3
214915_at	FLJ25476 protein	FLJ25476	149076	3
229198_at	ubiquitin specific peptidase 35	USP35	57558	3
218818_at	four and a half LIM domains 3	FHL3	2275	3
221873_at	zinc finger protein 143 (clone pHZ-1)	ZNF143	7702	3
201799_s_at	oxysterol binding protein	OSBP	5007	3
234563_at	Phosphodiesterase 3A, cGMP-inhibited	PDE3A	5139	3
208776_at	proteasome (prosome, macropain) 26S subunit, non-ATPase, 11	PSMD11	5717	3
33736_at	stomatin (EPB72)-like 1	STOML1	9399	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
212948_at	calmodulin binding transcription activator 2	CAMTA2	23125	3
221783_at	widely-interspaced zinc finger motifs	WIZ	58525	3
201136_at	proteolipid protein 2 (colonic epithelium-enriched)	PLP2	5355	3
218529_at	CD320 antigen	CD320	51293	3
205116_at	laminin, alpha 2 (merosin, congenital muscular dystrophy)	LAMA2	3908	3
205112_at	Phospholipase C, epsilon 1	PLCE1	51196	3
204384_at	golgi autoantigen, golgin subfamily a, 2	GOLGA2	2801	3
214649_s_at	myotubularin related protein 2	MTMR2	8898	3
209139_s_at	protein kinase, interferon-inducible double stranded RNA dependent activator	PRKRA	8575	3
223142_s_at	uridine-cytidine kinase 1	UCK1	83549	3
213758_at	cytochrome c oxidase subunit IV isoform 1	COX4I1	1327	3
235004_at	RNA binding motif protein 24	RBM24	221662	3
209781_s_at	KH domain containing, RNA binding, signal transduction associated 3	KHDRBS3	10656	3
225998_at	GRB2-associated binding protein 1	GAB1	2549	3
204241_at	acyl-Coenzyme A oxidase 3, pristanoyl	ACOX3	8310	3
226052_at	Bromodomain containing 4	BRD4	23476	3
215030_at	G-rich RNA sequence binding factor 1	GRSF1	2926	3
200895_s_at	FK506 binding protein 4, 59kDa	FKBP4	2288	3
203557_s_at	6-pyruvoyl-tetrahydropterin synthase/dimerization cofactor of hepatocyte nuclear factor 1 alpha (TCF1)	PCBD1	5092	3
226196_s_at	MGC16028 similar to RIKEN cDNA 1700019E19 gene	MGC16028	112752	3
214097_at	ribosomal protein S21	RPS21	6227	3
224689_at	mannosidase, beta A, lysosomal-like	MANBAL	63905	3
203456_at	PRA1 domain family, member 2	PRAF2	11230	3
1557553_at	Protein phosphatase 1, regulatory (inhibitor) subunit 12B	PPP1R12B	4660	3
211450_s_at	mutS homolog 6 (E. coli)	MSH6	2956	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201459_at	RuvB-like 2 (E. coli)	RUVBL2	10856	3
224078_at	hippocampus abundant gene transcript-like 2	HIATL2	84278	3
1565717_s_at	fusion (involved in t(12;16) in malignant liposarcoma)	FUS	2521	3
229377_at	Growth hormone regulated TBC protein 1	GRTP1	79774	3
202137_s_at	zinc finger, MYND domain containing 11	ZMYND11	10771	3
227388_at	tumor suppressor candidate 1	TUSC1	286319	3
213587_s_at	ATPase, H+ transporting V0 subunit E isoform 2-like (rat)	ATP6V0E2L	155066	3
215016_x_at	dystonin	DST	667	3
224671_at	mitochondrial ribosomal protein L10	MRPL10	124995	3
200820_at	proteasome (prosome, macropain) 26S subunit, non-ATPase, 8	PSMD8	5714	3
209129_at	thyroid hormone receptor interactor 6	TRIP6	7205	3
201679_at	arsenate resistance protein ARS2	ARS2	51593	3
205775_at	family with sequence similarity 50, member B	FAM50B	26240	3
217753_s_at	ribosomal protein S26 ; 40S ribosomal protein S26-like ; similar to 40S ribosomal protein S26	RPS26	400156	3
225782_at	methionine sulfoxide reductase B3	MSRB3	253827	3
223852_s_at	serine/threonine kinase 40	STK40	83931	3
200646_s_at	nucleobindin 1	NUCB1	4924	3
224719_s_at	likely ortholog of mouse gene rich cluster, C10 gene	GRCC10	113246	3
235014_at	hypothetical protein LOC147727	LOC147727	147727	3
218553_s_at	potassium channel tetramerisation domain containing 15	KCTD15	79047	3
206972_s_at	G protein-coupled receptor 161	GPR161	23432	3
207415_at	phospholipase A2 receptor 1, 180kDa	PLA2R1	22925	3
205125_at	phospholipase C, delta 1	PLCD1	5333	3
222524_s_at	ankyrin repeat and SOCS box-containing 6	ASB6	140459	3
227426_at	Son of sevenless homolog 1 (Drosophila)	SOS1	6654	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
210640_s_at	G protein-coupled receptor 30	GPR30	2852	3
232780_s_at	zinc finger protein 691	ZNF691	51058	3
231183_s_at	Jagged 1 (Alagille syndrome)	JAG1	182	3
228776_at	gap junction protein, alpha 7, 45kDa (connexin 45)	GJA7	10052	3
204400_at	embryonal Fyn-associated substrate	EFS	10278	3
207622_s_at	ATP-binding cassette, sub-family F (GCN20), member 2	ABCF2	10061	3
205084_at	B-cell receptor-associated protein 29	BCAP29	55973	3
222860_s_at	platelet derived growth factor D	PDGFD	80310	3
226615_at	Xenotropic and polytropic retrovirus receptor	XPR1	9213	3
225480_at	chromosome 1 open reading frame 122	C1orf122	127687	3
214002_at	myosin, light polypeptide 6, alkali, smooth muscle and non-muscle	MYL6	4637	3
211954_s_at	RAN binding protein 5	RANBP5	3843	3
200611_s_at	WD repeat domain 1	WDR1	9948	3
230656_s_at	cirrhosis, autosomal recessive 1A (cirhin)	CIRH1A	84916	3
211759_x_at	cytoskeleton associated protein 1 ; cytoskeleton associated protein 1	CKAP1	1155	3
204905_s_at	eukaryotic translation elongation factor 1 epsilon 1	EEF1E1	9521	3
213490_s_at	mitogen-activated protein kinase kinase 2	MAP2K2	5605	3
217795_s_at	transmembrane protein 43	TMEM43	79188	3
231961_at	RNA binding protein with multiple splicing	RBPMS	11030	3
202916_s_at	family with sequence similarity 20, member B	FAM20B	9917	3
217820_s_at	enabled homolog (Drosophila)	ENAH	55740	3
207749_s_at	protein phosphatase 2 (formerly 2A), regulatory subunit B'', alpha	PPP2R3A	5523	3
206356_s_at	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide, olfactory type	GNAL	2774	3
204042_at	WAS protein family, member 3	WASF3	10810	3
209355_s_at	phosphatidic acid phosphatase type 2B	PPAP2B	8613	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
200956_s_at	structure specific recognition protein 1	SSRP1	6749	3
212891_s_at	growth arrest and DNA-damage-inducible, gamma interacting protein 1	GADD45GIP1	90480	3
202550_s_at	VAMP (vesicle-associated membrane protein)-associated protein B and C	VAPB	9217	3
227992_s_at	hypothetical protein LOC147650	LOC147650	147650	3
201538_s_at	dual specificity phosphatase 3 (vaccinia virus phosphatase VH1-related)	DUSP3	1845	3
202571_s_at	discs, large (Drosophila) homolog-associated protein 4	DLGAP4	22839	3
220964_s_at	RAB1B, member RAS oncogene family ; RAB1B, member RAS oncogene family	RAB1B	81876	3
217923_at	penta-EF-hand domain containing 1	PEF1	553115	3
209522_s_at	carnitine acetyltransferase	CRAT	1384	3
204790_at	SMAD, mothers against DPP homolog 7 (Drosophila)	SMAD7	4092	3
211598_x_at	vasoactive intestinal peptide receptor 2 ; vasoactive intestinal peptide receptor 2	VIPR2	7434	3
212729_at	discs, large homolog 3 (neuroendocrine-dlg, Drosophila)	DLG3	1741	3
234192_s_at	G kinase anchoring protein 1	GKAP1	80318	3
214177_s_at	pre-B-cell leukemia transcription factor interacting protein 1	PBXIP1	57326	3
222318_at	FLJ45850 protein	FLJ45850	388569	3
212765_at	calmodulin regulated spectrin-associated protein 1-like 1	CAMSAP1L1	23271	3
202587_s_at	adenylate kinase 1	AK1	203	3
202069_s_at	isocitrate dehydrogenase 3 (NAD+) alpha	IDH3A	3419	3
209406_at	BCL2-associated athanogene 2	BAG2	9532	3
212875_s_at	chromosome 21 open reading frame 25	C21orf25	25966	3
212755_at	KIAA1040 protein	KIAA1040	23041	3
230790_x_at	checkpoint suppressor 1	CHES1	1112	3
208456_s_at	related RAS viral (r-ras) oncogene homolog 2	RRAS2	22800	3
225533_at	PHD finger protein 19	PHF19	26147	3
212739_s_at	non-metastatic cells 4, protein expressed in	NME4	4833	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
227064_at	ankyrin repeat domain 40	ANKRD40	91369	3
212504_at	KIAA0934	KIAA0934	22982	3
222165_x_at	chromosome 9 open reading frame 16	C9orf16	79095	3
208702_x_at	amyloid beta (A4) precursor-like protein 2	APLP2	334	3
225860_at	hypothetical LOC400843	LOC400843	400843	3
233130_at	Thyroid hormone receptor, beta (erythroblastic leukemia viral (v-erb-a) oncogene homolog 2, avian)	THRB	7068	3
204424_s_at	LIM domain only 3 (rhombotin-like 2)	LMO3	55885	3
224844_at	KIAA1458 protein	KIAA1458	57606	3
202123_s_at	v-abl Abelson murine leukemia viral oncogene homolog 1	ABL1	25	3
1556136_at	hypothetical protein LOC340156	LOC340156	340156	3
201667_at	gap junction protein, alpha 1, 43kDa (connexin 43)	GJA1	2697	3
203404_at	armadillo repeat containing, X-linked 2	ARMCX2	9823	3
223894_s_at	fused toes homolog (mouse)	FTS	64400	3
232950_s_at	phosphatidylinositol transfer protein, membrane-associated 2	PITPNM2	57605	3
202570_s_at	discs, large (Drosophila) homolog-associated protein 4	DLGAP4	22839	3
218641_at	hypothetical protein MGC3032	MGC3032	65998	3
226653_at	MAP/microtubule affinity-regulating kinase 1	MARK1	4139	3
219090_at	solute carrier family 24 (sodium/potassium/calcium exchanger), member 3	SLC24A3	57419	3
223129_x_at	myosin regulatory light chain interacting protein	MYLIP	29116	3
208951_at	aldehyde dehydrogenase 7 family, member A1	ALDH7A1	501	3
213696_s_at	mediator of RNA polymerase II transcription, subunit 8 homolog (yeast)	MED8	112950	3
229793_at	Apobec-1 complementation factor	ACF	29974	3
222482_at	single stranded DNA binding protein 3	SSBP3	23648	3
201270_x_at	NudC domain containing 3	NUDCD3	23386	3
201903_at	ubiquinol-cytochrome c reductase core protein I	UQCRC1	7384	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
218942_at	phosphatidylinositol-4-phosphate 5-kinase, type II, gamma	PIP5K2C	79837	3
213262_at	spastic ataxia of Charlevoix-Saguenay (sacsin)	SACS	26278	3
243555_at	Endothelin receptor type A	EDNRA	1909	3
203711_s_at	3-hydroxyisobutyryl-Coenzyme A hydrolase	HIBCH	26275	3
202124_s_at	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 3	ALS2CR3	66008	3
241926_s_at	v-ets erythroblastosis virus E26 oncogene like (avian)	ERG	2078	3
201418_s_at	SRY (sex determining region Y)-box 4	SOX4	6659	3
220770_s_at	transposon-derived Buster3 transposase-like	LOC63920	63920	3
211571_s_at	chondroitin sulfate proteoglycan 2 (versican)	CSPG2	1462	3
212686_at	protein phosphatase 1H (PP2C domain containing)	PPM1H	57460	3
228948_at	EPH receptor A4	EPHA4	2043	3
1569104_a_at	Protein tyrosine phosphatase, non-receptor type 23	PTPN23	25930	3
221486_at	endosulfine alpha	ENSA	2029	3
1566785_x_at	Ribosomal protein S7	NSF	4905	3
227386_s_at	cDNA DKFZp434C184 gene	TTMB	399474	3
202734_at	thyroid hormone receptor interactor 10	TRIP10	9322	3
204843_s_at	protein kinase, cAMP-dependent, regulatory, type II, alpha	PRKAR2A	5576	3
208963_x_at	fatty acid desaturase 1	FADS1	3992	3
213325_at	poliovirus receptor-related 3	PVRL3	25945	3
202522_at	phosphatidylinositol transfer protein, beta	PITPNB	23760	3
225094_at	PR/SET domain containing protein 8	SET8	387893	3
227107_at	Pannexin 1	PANX1	24145	3
202893_at	unc-13 homolog B (C. elegans)	UNC13B	10497	3
203411_s_at	lamin A/C	LMNA	4000	3
226484_at	zinc finger protein 651	ZNF651	92999	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
228455_at	Solute carrier family 16 (monocarboxylic acid transporters), member 4	SLC16A4	9122	3
209379_s_at	KIAA1128	KIAA1128	54462	3
209482_at	processing of precursor 7, ribonuclease P subunit (S. cerevisiae)	POP7	10248	3
201431_s_at	dihydropyrimidinase-like 3	DPYSL3	1809	3
223008_s_at	chromosome 9 open reading frame 5	C9orf5	23731	3
225275_at	EGF-like repeats and discoidin I-like domains 3	EDIL3	10085	3
214564_s_at	protocadherin gamma subfamily C, 3	PCDHGC3	5098	3
222571_at	ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)	ST6GALNAC6	30815	3
236118_at	hypothetical LOC201484	LOC201484	201484	3
229811_at	Adhesion regulating molecule 1	ADRM1	11047	3
217787_s_at	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2)	GALNT2	2590	3
244680_at	glycine receptor, beta	GLRB	2743	3
210022_at	polycomb group ring finger 1	PCGF1	84759	3
210372_s_at	tumor protein D52-like 1	TPD52L1	7164	3
205357_s_at	angiotensin II receptor, type 1	AGTR1	185	3
204718_at	EPH receptor B6	EPHB6	2051	3
210991_s_at	regulating synaptic membrane exocytosis 3	RIMS3	9783	3
1559360_at	Nuclear RNA-binding protein, putative	EFNA5	1946	3
221762_s_at	chromosome 20 open reading frame 67	C20orf67	63935	3
212480_at	KIAA0376 protein	KIAA0376	23384	3
226033_at	ubiquitin specific peptidase 31	USP31	57478	3
216210_x_at	TRIO and F-actin binding protein	TRIOBP	11078	3
205991_s_at	paired related homeobox 1	PRRX1	5396	3
230121_at	SERTA domain containing 4	SERTAD4	56256	3
233005_at	Chromosome 1 open reading frame 181	FLJ20729	54680	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
209834_at	carbohydrate (chondroitin 6) sulfotransferase 3	CHST3	9469	3
224792_at	tankyrase 1 binding protein 1, 182kDa	TNKS1BP1	85456	3
206742_at	c-fos induced growth factor (vascular endothelial growth factor D)	FIGF	2277	3
226722_at	family with sequence similarity 20, member C	FAM20C	56975	3
1553678_a_at	integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	ITGB1	3688	3
1554791_a_at	hypothetical protein FLJ23861	FLJ23861	151050	3
225119_at	chromatin modifying protein 4B	CHMP4B	128866	3
235631_at	Discoidin domain receptor family, member 2	DDR2	4921	3
224162_s_at	F-box protein 31	FBXO31	79791	3
229590_at	Ribosomal protein L13	RPL13	6137	3
212358_at	CLIP-170-related protein	CLIPR-59	25999	3
213435_at	SATB family member 2	SATB2	23314	3
212775_at	obscurin-like 1	OBSL1	23363	3
202927_at	protein (peptidyl-prolyl cis/trans isomerase) NIMA-interacting 1	PIN1	5300	3
1556787_s_at	Phosphodiesterase 5A, cGMP-specific	PDE5A	8654	3
201828_x_at	CAAX box 1	CXX1	8933	3
202135_s_at	ARP1 actin-related protein 1 homolog B, centractin beta (yeast)	ACTR1B	10120	3
205172_x_at	clathrin, light polypeptide (Lcb)	CLTB	1212	3
217903_at	striatin, calmodulin binding protein 4	STRN4	29888	3
207738_s_at	NCK-associated protein 1	NCKAP1	10787	3
206929_s_at	nuclear factor I/C (CCAAT-binding transcription factor)	NFIC	4782	3
209612_s_at	alcohol dehydrogenase IB (class I), beta polypeptide	ADH1B	125	3
226656_at	cartilage associated protein	CRTAP	10491	3
225874_at	LOC124402	LOC124402	124402	3
226198_at	target of myb1-like 2 (chicken)	TOM1L2	146691	3

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
222065_s_at	flightless I homolog (Drosophila)	FLII	2314	3
225025_at	immunoglobulin superfamily, member 8	IGSF8	93185	3
218518_at	chromosome 5 open reading frame 5	C5orf5	51306	3
203160_s_at	ring finger protein 8	RNF8	9025	3
213622_at	collagen, type IX, alpha 2	COL9A2	1298	3
228845_at	hypothetical protein LOC196463	LOC196463	196463	3
201397_at	phosphoglycerate dehydrogenase	PHGDH	26227	3
227096_at	hypothetical transmembrane protein SBBI54	SBBI54	126119	3
234193_at	Hypothetical protein FLJ10770	KIAA1579	55225	3
224804_s_at	chromosome 15 open reading frame 17	C15orf17	57184	3
235550_at	ASAP	FLJ21159	79884	3
212853_at	DCN1, defective in cullin neddylation 1, domain containing 4 (S. cerevisiae)	DCUN1D4	23142	3
208248_x_at	amyloid beta (A4) precursor-like protein 2	APLP2	334	3
1558522_at	Membrane protein, palmitoylated 6 (MAGUK p55 subfamily member 6)	MPP6	51678	3
214717_at	hypothetical protein DKFZp434H1419	DKFZp434H1419	150967	3
210829_s_at	single-stranded DNA binding protein 2	SSBP2	23635	3
1553113_s_at	Cyclin-dependent kinase 8	CDK8	1024	3
212548_s_at	KIAA0826	KIAA0826	23045	3
211208_s_at	calcium/calmodulin-dependent serine protein kinase (MAGUK family)	CASK	8573	3
223421_at	cysteine/histidine-rich 1	CYHR1	50626	3
203823_at	regulator of G-protein signalling 3	RGS3	5998	3
1564331_at	hypothetical protein LOC162993	LOC162993	162993	2
208699_x_at	transketolase (Wernicke-Korsakoff syndrome)	TKT	7086	2
227153_at	IMP2 inner mitochondrial membrane peptidase-like (S. cerevisiae)	IMMP2L	83943	2
208016_s_at	angiotensin II receptor, type 1	AGTR1	185	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
211622_s_at	ADP-ribosylation factor 3 ; ADP-ribosylation factor 3	ARF3	377	2
206414_s_at	development and differentiation enhancing factor 2	DDEF2	8853	2
201764_at	hypothetical protein MGC5576	MGC5576	79022	2
243618_s_at	Hypothetical protein LOC152485	LOC152485	152485	2
200795_at	SPARC-like 1 (mast9, hevin)	SPARCL1	8404	2
211602_s_at	transient receptor potential cation channel, subfamily C, member 1	TRPC1	7220	2
214011_s_at	hypothetical protein HSPC111	HSPC111	51491	2
213901_x_at	RNA binding motif protein 9	RBM9	23543	2
202133_at	WW domain containing transcription regulator 1	WWTR1	25937	2
202804_at	ATP-binding cassette, sub-family C (CFTR/MRP), member 1	ABCC1	4363	2
226795_at	Leucine-rich repeats and calponin homology (CH) domain containing 1	LRCH1	23143	2
205166_at	calpain 5	CAPN5	726	2
202353_s_at	proteasome (prosome, macropain) 26S subunit, non-ATPase, 12	PSMD12	5718	2
1558027_s_at	protein kinase, AMP-activated, beta 2 non-catalytic subunit	PRKAB2	5565	2
203045_at	ninjurin 1	NINJ1	4814	2
204242_s_at	acyl-Coenzyme A oxidase 3, pristanoyl	ACOX3	8310	2
202309_at	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 1	MTHFD1	4522	2
1553101_a_at	hypothetical protein FLJ20308	FLJ20308	54890	2
211979_at	G protein-coupled receptor 107	GPR107	57720	2
200940_s_at	arginine-glutamic acid dipeptide (RE) repeats	RERE	473	2
219496_at	chromosome 2 open reading frame 26	C2orf26	65124	2
218679_s_at	vacuolar protein sorting 28 (yeast)	VPS28	51160	2
200878_at	endothelial PAS domain protein 1	EPAS1	2034	2
202756_s_at	glypican 1	GPC1	2817	2
232129_s_at	leucine zipper, putative tumor suppressor 2	LZTS2	84445	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
228046_at	Hypothetical protein LOC152485	LOC152485	152485	2
226554_at	zinc finger and BTB domain containing 7A	ZBTB7A	51341	2
226428_at	transportin 2 (importin 3, karyopherin beta 2b)	TNPO2	30000	2
208847_s_at	alcohol dehydrogenase 5 (class III), chi polypeptide	ADH5	128	2
212610_at	protein tyrosine phosphatase, non-receptor type 11 (Noonan syndrome 1)	PTPN11	5781	2
239762_at	hypothetical protein LOC286437	LOC286437	286437	2
208132_x_at	HLA-B associated transcript 2	BAT2	7916	2
201984_s_at	epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	EGFR	1956	2
203259_s_at	HD domain containing 2	HDDC2	51020	2
232994_s_at	Rho-guanine nucleotide exchange factor	RGNEF	64283	2
203551_s_at	COX11 homolog, cytochrome c oxidase assembly protein (yeast)	COX11	1353	2
214894_x_at	microtubule-actin crosslinking factor 1	MACF1	23499	2
205417_s_at	dystroglycan 1 (dystrophin-associated glycoprotein 1)	DAG1	1605	2
223033_s_at	SCY1-like 1 (S. cerevisiae)	SCYL1	57410	2
238568_s_at	Chromosome 18 open reading frame 8	C18orf8	29919	2
210276_s_at	TRIO and F-actin binding protein	TRIOBP	11078	2
229412_at	Taube nuss homolog (mouse)	TBN	129685	2
223112_s_at	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 10, 22kDa	NDUFB10	4716	2
244753_at	Actinin, alpha 4	ACTN4	81	2
203958_s_at	zinc finger and BTB domain containing 40	ZBTB40	9923	2
225498_at	chromatin modifying protein 4B	CHMP4B	128866	2
201908_at	dishevelled, dsh homolog 3 (Drosophila)	DVL3	1857	2
241809_at	chromosome 1 open reading frame 183	C1orf183	55924	2
1552660_a_at	hypothetical protein FLJ11193	FLJ11193	55322	2
200812_at	chaperonin containing TCP1, subunit 7 (eta)	CCT7	10574	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
200771_at	laminin, gamma 1 (formerly LAMB2)	LAMC1	3915	2
201804_x_at	cytoskeleton associated protein 1	CKAP1	1155	2
230291_s_at	Nuclear factor I/B	NFIB	4781	2
227197_at	Src homology 3 domain-containing guanine nucleotide exchange factor	SGEF	26084	2
228882_at	tubby homolog (mouse)	TUB	7275	2
219855_at	nudix (nucleoside diphosphate linked moiety X)-type motif 11	NUDT11	55190	2
223141_at	uridine-cytidine kinase 1	UCK1	83549	2
227657_at	ring finger protein 150	RNF150	57484	2
209044_x_at	splicing factor 3b, subunit 4, 49kDa	SF3B4	10262	2
231750_at	protocadherin beta 4	PCDHB4	56131	2
221047_s_at	MAP/microtubule affinity-regulating kinase 1	MARK1	4139	2
217511_at	Kazal-type serine peptidase inhibitor domain 1	KAZALD1	81621	2
235857_at	potassium channel tetramerisation domain containing 11	KCTD11	147040	2
213701_at	hypothetical protein DKFZp434N2030	DKFZp434N2030	91298	2
230364_at	choline phosphotransferase 1	CHPT1	56994	2
213242_x_at	KIAA0284	KIAA0284	283638	2
212865_s_at	collagen, type XIV, alpha 1 (undulin)	COL14A1	7373	2
223879_s_at	oxidation resistance 1	OXR1	55074	2
202290_at	PDGFA associated protein 1	PDAP1	11333	2
223854_at	protocadherin beta 10	PCDHB10	56126	2
212032_s_at	prostate tumor overexpressed gene 1	PTOV1	53635	2
201770_at	small nuclear ribonucleoprotein polypeptide A	SNRPA	6626	2
233536_at	KIAA1713	KIAA1713	80816	2
1558604_a_at	MRNA; clone CD 43T7			2
214201_x_at	HLA-B associated transcript 2	BAT2	7916	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
220319_s_at	myosin regulatory light chain interacting protein	MYLIP	29116	2
212004_at	chromosome 1 open reading frame 144	C1orf144	26099	2
224931_at	solute carrier family 41, member 3	SLC41A3	54946	2
204398_s_at	echinoderm microtubule associated protein like 2	EML2	24139	2
212698_s_at	septin 10	Sep-10	151011	2
238753_at	Frequenin homolog (Drosophila)	FREQ	23413	2
232270_at	Chromosome 9 open reading frame 3	C9orf3	84909	2
203874_s_at	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily a, member 1	SMARCA1	6594	2
238006_at	SIN3 homolog A, transcription regulator (yeast)	SIN3A	25942	2
209356_x_at	EGF-containing fibulin-like extracellular matrix protein 2	EFEMP2	30008	2
217937_s_at	histone deacetylase 7A	HDAC7A	51564	2
218903_s_at	hypothetical protein MGC2731	MGC2731	79035	2
217782_s_at	G protein pathway suppressor 1	GPS1	2873	2
238458_at	EF-hand domain family, member A2	EFHA2	286097	2
225245_x_at	H2A histone family, member J	H2AFJ	55766	2
200049_at	MYST histone acetyltransferase 2 ; MYST histone acetyltransferase 2	MYST2	11143	2
223089_at	transmembrane protein vezatin	VEZATIN	55591	2
225975_at	protocadherin 18	PCDH18	54510	2
244476_at	Tight junction protein 1 (zona occludens 1)	TJP1	7082	2
1554747_a_at	septin 2	Sep-02	4735	2
222986_s_at	scotin	SCOTIN	51246	2
201603_at	protein phosphatase 1, regulatory (inhibitor) subunit 12A	PPP1R12A	4659	2
214247_s_at	dickkopf homolog 3 (Xenopus laevis)	DKK3	27122	2
200950_at	actin related protein 2/3 complex, subunit 1A, 41kDa	ARPC1A	10552	2
201897_s_at	CDC28 protein kinase regulatory subunit 1B	CKS1B	1163	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
1555851_s_at	selenoprotein W, 1	SEPW1	6415	2
1555500_s_at	SLC2A4 regulator	SLC2A4RG	56731	2
206284_x_at	clathrin, light polypeptide (Lcb)	CLTB	1212	2
1554159_a_at	zinc finger, MYND domain containing 11	ZMYND11	10771	2
203303_at	t-complex-associated-testis-expressed 1-like	TCTE1L	6990	2
209200_at	MADS box transcription enhancer factor 2, polypeptide C (myocyte enhancer factor 2C)	MEF2C	4208	2
201968_s_at	phosphoglucomutase 1	PGM1	5236	2
213470_s_at	heterogeneous nuclear ribonucleoprotein H1 (H)	HNRPH1	3187	2
211926_s_at	myosin, heavy polypeptide 9, non-muscle	MYH9	4627	2
201403_s_at	microsomal glutathione S-transferase 3	MGST3	4259	2
203109_at	ubiquitin-conjugating enzyme E2M (UBC12 homolog, yeast)	UBE2M	9040	2
208700_s_at	transketolase (Wernicke-Korsakoff syndrome)	TKT	7086	2
215222_x_at	microtubule-actin crosslinking factor 1	MACF1	23499	2
223471_at	RAB3A interacting protein (rabin3)	RAB3IP	117177	2
39548_at	neuronal PAS domain protein 2	NPAS2	4862	2
35666_at	sema domain, immunoglobulin domain (Ig), short basic domain, secreted, (semaphorin) 3F	SEMA3F	6405	2
209586_s_at	prune homolog (Drosophila)	PRUNE	58497	2
201022_s_at	destrin (actin depolymerizing factor)	DSTN	11034	2
244070_at	spectrin repeat containing, nuclear envelope 1	SYNE1	23345	2
224318_s_at	hypothetical protein FLJ10081	FLJ10081	55683	2
225005_at	PHD finger protein 13	PHF13	148479	2
209381_x_at	splicing factor 3a, subunit 2, 66kDa	SF3A2	8175	2
210010_s_at	solute carrier family 25 (mitochondrial carrier; citrate transporter), member 1	SLC25A1	6576	2
40837_at	transducin-like enhancer of split 2 (E(sp1) homolog, Drosophila)	TLE2	7089	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
225471_s_at	v-akt murine thymoma viral oncogene homolog 2	AKT2	208	2
212110_at	solute carrier family 39 (zinc transporter), member 14	SLC39A14	23516	2
200988_s_at	proteasome (prosome, macropain) activator subunit 3 (PA28 gamma; Ki)	PSME3	10197	2
241395_at	Death effector domain containing	DEDD	9191	2
212034_s_at	exocyst complex component 7	EXOC7	23265	2
225260_s_at	mitochondrial ribosomal protein L32	MRPL32	64983	2
206814_at	nerve growth factor, beta polypeptide	NGFB	4803	2
212244_at	glutamate receptor, ionotropic, N-methyl D-aspartate-like 1A ; GRINL1A combined protein	GRINL1A	145781	2
224941_at	pregnancy-associated plasma protein A, pappalysin 1	PAPPA	5069	2
217831_s_at	NSFL1 (p97) cofactor (p47)	NSFL1C	55968	2
219268_at	ethanolamine kinase 2	ETNK2	55224	2
223690_at	latent transforming growth factor beta binding protein 2	LTBP2	4053	2
222064_s_at	hypothetical protein MGC2744	MGC2744	80755	2
225464_at	FERM domain containing 6	FRMD6	122786	2
222400_s_at	membrane-type 1 matrix metalloproteinase cytoplasmic tail binding protein-1	MTCBP-1	55256	2
1562863_at	Exostoses (multiple) 1	EXT1	2131	2
238454_at	zinc finger protein 540	ZNF540	163255	2
220597_s_at	ADP-ribosylation-like factor 6 interacting protein 4	ARL6IP4	51329	2
36554_at	acetylserotonin O-methyltransferase-like	ASMTL	8623	2
202806_at	drebrin 1	DBN1	1627	2
219394_at	phosphatidylglycerophosphate synthase	PGS1	9489	2
205527_s_at	gem (nuclear organelle) associated protein 4	GEMIN4	50628	2
202590_s_at	pyruvate dehydrogenase kinase, isoenzyme 2	PDK2	5164	2
207722_s_at	BTB (POZ) domain containing 2	BTBD2	55643	2
219520_s_at	KIAA1280 protein	KIAA1280	55841	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
205079_s_at	multiple PDZ domain protein	MPDZ	8777	2
228093_at	Zinc finger protein 599	ZNF599	148103	2
224982_at	AKT1 substrate 1 (proline-rich)	AKT1S1	84335	2
242985_x_at	ring finger protein 180	RNF180	285671	2
225536_at	transmembrane protein 54	TMEM54	113452	2
218284_at	SMAD, mothers against DPP homolog 3 (Drosophila)	SMAD3	4088	2
213244_at	secretory carrier membrane protein 4	SCAMP4	113178	2
242697_at	zinc finger protein 540	ZNF540	163255	2
200990_at	tripartite motif-containing 28	TRIM28	10155	2
225751_at	RNA binding motif protein 17	RBM17	84991	2
208670_s_at	CREBBP/EP300 inhibitor 1	CRI1	23741	2
209337_at	PC4 and SFRS1 interacting protein 1	PSIP1	11168	2
200980_s_at	pyruvate dehydrogenase (lipoamide) alpha 1	PDHA1	5160	2
201436_at	eukaryotic translation initiation factor 4E	EIF4E	1977	2
208611_s_at	spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	SPTAN1	6709	2
225298_at	myofibrillogenesis regulator 1	MR-1	25953	2
201125_s_at	integrin, beta 5	ITGB5	3693	2
212367_at	fem-1 homolog b (C. elegans)	FEM1B	10116	2
224774_s_at	neuron navigator 1	NAV1	89796	2
212216_at	prolyl endopeptidase-like	PREPL	9581	2
209252_at	histidyl-tRNA synthetase-like	HARSL	23438	2
217722_s_at	neugrin, neurite outgrowth associated	NGRN	51335	2
224876_at	hypothetical protein FLJ37562	FLJ37562	134553	2
221542_s_at	SPFH domain family, member 2	SPFH2	11160	2
202117_at	Rho GTPase activating protein 1	ARHGAP1	392	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
202624_s_at	calcineurin binding protein 1	CABIN1	23523	2
207623_at	ATP-binding cassette, sub-family F (GCN20), member 2	ABCF2	10061	2
225623_at	KIAA1737	KIAA1737	85457	2
226809_at	similar to hypothetical protein A230046P18; cDNA sequence BC055759	FLJ30428	150519	2
205794_s_at	neuro-oncological ventral antigen 1	NOVA1	4857	2
210844_x_at	catenin (cadherin-associated protein), alpha 1, 102kDa	CTNNA1	1495	2
207838_x_at	pre-B-cell leukemia transcription factor interacting protein 1	PBXIP1	57326	2
201335_s_at	Rho guanine nucleotide exchange factor (GEF) 12	ARHGEF12	23365	2
220134_x_at	chromosome 1 open reading frame 78	C1orf78	55194	2
204811_s_at	calcium channel, voltage-dependent, alpha 2/delta subunit 2	CACNA2D2	9254	2
221867_at	Nedd4 binding protein 1	N4BP1	9683	2
207469_s_at	pirin (iron-binding nuclear protein)	PIR	8544	2
201507_at	prefoldin 1	PFDN1	5201	2
238009_at	SRY (sex determining region Y)-box 5	SOX5	6660	2
232073_at	protein tyrosine phosphatase, receptor type, f polypeptide (PTPRF), interacting protein (liprin), alpha 2	PPFIA2	8499	2
204222_s_at	GLI pathogenesis-related 1 (glioma)	GLIPR1	11010	2
201271_s_at	RNA binding protein, autoantigenic (hnRNP-associated with lethal yellow homolog (mouse))	RALY	22913	2
224697_at	WD repeat domain 22	WDR22	8816	2
212015_x_at	polypyrimidine tract binding protein 1	PTBP1	5725	2
204964_s_at	sarcospan (Kras oncogene-associated gene)	SSPN	8082	2
212186_at	acetyl-Coenzyme A carboxylase alpha	ACACA	31	2
226731_at	Pelota homolog (Drosophila)	PELO	53918	2
203105_s_at	dynamin 1-like	DNM1L	10059	2
219491_at	leucine rich repeat and fibronectin type III domain containing 4	LRFN4	78999	2
217854_s_at	polymerase (RNA) II (DNA directed) polypeptide E, 25kDa	POLR2E	5434	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201932_at	leucine rich repeat containing 41	LRRC41	10489	2
234942_s_at	deoxynucleotidyltransferase, terminal, interacting protein 1	DNTTIP1	116092	2
224506_s_at	phosphatidic acid phosphatase type 2 domain containing 3	PPAPDC3	84814	2
225905_s_at	ST3 beta-galactoside alpha-2,3-sialyltransferase 3	ST3GAL3	6487	2
213944_x_at	guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	2
213455_at	hypothetical LOC283677	LOC283677	283677	2
205345_at	BRCA1 associated RING domain 1	BARD1	580	2
201334_s_at	Rho guanine nucleotide exchange factor (GEF) 12	ARHGEF12	23365	2
218694_at	armadillo repeat containing, X-linked 1	ARMCX1	51309	2
218861_at	ring finger protein 25	RNF25	64320	2
211932_at	heterogeneous nuclear ribonucleoprotein A3	HNRPA3	220988	2
203430_at	heme binding protein 2	HEBP2	23593	2
243894_at	solute carrier family 41, member 2	SLC41A2	84102	2
243305_at	Kelch domain containing 5	KIAA1340	57542	2
223287_s_at	forkhead box P1	FOXP1	27086	2
212932_at	RAB3 GTPase activating protein subunit 1 (catalytic)	RAB3GAP1	22930	2
226977_at	similar to bovine IgA regulatory protein	LOC492311	492311	2
203794_at	CDC42 binding protein kinase alpha (DMPK-like)	CDC42BPA	8476	2
218477_at	transmembrane protein 14A	TMEM14A	28978	2
214726_x_at	adducin 1 (alpha)	ADD1	118	2
210428_s_at	hepatocyte growth factor-regulated tyrosine kinase substrate	HGS	9146	2
205282_at	low density lipoprotein receptor-related protein 8, apolipoprotein e receptor	LRP8	7804	2
227019_at	hypothetical gene supported by AK125122	LOC400793	400793	2
224913_s_at	translocase of inner mitochondrial membrane 50 homolog (yeast)	TIMM50	92609	2
228378_at	hypothetical protein DKFZp434N2030	DKFZp434N2030	91298	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201158_at	N-myristoyltransferase 1	NMT1	4836	2
212126_at	Chromobox homolog 5 (HP1 alpha homolog, Drosophila)	CBX5	23468	2
229488_at	Zinc finger, A20 domain containing 1	ZA20D1	56957	2
210115_at	ribosomal protein L39-like	RPL39L	116832	2
213489_at	Microtubule-associated protein, RP/EB family, member 2	MAPRE2	10982	2
212009_s_at	stress-induced-phosphoprotein 1 (Hsp70/Hsp90-organizing protein)	STIP1	10963	2
230757_at	FLJ44796 protein	FLJ44796	401209	2
200784_s_at	low density lipoprotein-related protein 1 (alpha-2-macroglobulin receptor)	LRP1	4035	2
224698_at	family with sequence similarity 62 (C2 domain containing) member B	FAM62B	57488	2
204875_s_at	GDP-mannose 4,6-dehydratase	GMDS	2762	2
227286_at	hypothetical protein FLJ90652	FLJ90652	283899	2
228857_at	hypothetical protein LOC285831	LOC285831	285831	2
202959_at	methylmalonyl Coenzyme A mutase	MUT	4594	2
203085_s_at	transforming growth factor, beta 1 (Camurati-Engelmann disease)	TGFB1	7040	2
204389_at	monoamine oxidase A	MAOA	4128	2
201540_at	four and a half LIM domains 1	FHL1	2273	2
201241_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 1	DDX1	1653	2
220917_s_at	WD repeat domain 19	WDR19	57728	2
217784_at	SNARE protein Ykt6	YKT6	10652	2
201330_at	arginyl-tRNA synthetase	RARS	5917	2
225930_at	NFKB inhibitor interacting Ras-like 1	NKIRAS1	28512	2
1555233_at	ras homolog gene family, member J	RHOJ	57381	2
203221_at	transducin-like enhancer of split 1 (E(sp1) homolog, Drosophila)	TLE1	7088	2
201066_at	cytochrome c-1	CYC1	1537	2
219020_at	HS1-binding protein 3	HS1BP3	64342	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
226322_at	ARG99 protein	ARG99	83857	2
215493_x_at	butyrophilin, subfamily 2, member A1	BTN2A1	11120	2
225999_at	family with sequence similarity 80, member B	FAM80B	57494	2
226749_at	mitochondrial ribosomal protein S9	MRPS9	64965	2
200759_x_at	nuclear factor (erythroid-derived 2)-like 1	NFE2L1	4779	2
225958_at	polyhomeotic-like 1 (Drosophila)	PHC1	1911	2
201215_at	plastin 3 (T isoform)	PLS3	5358	2
228438_at	Musculin (activated B-cell factor-1)	MSC	8989	2
217963_s_at	nerve growth factor receptor (TNFRSF16) associated protein 1	NGFRAP1	27018	2
223991_s_at	UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2)	GALNT2	2590	2
224772_at	neuron navigator 1	NAV1	89796	2
223294_at	chromosome X open reading frame 26	CXorf26	51260	2
228393_s_at	zinc finger protein 302	ZNF302	55900	2
206721_at	chromosome 1 open reading frame 114	C1orf114	57821	2
1554089_s_at	Shwachman-Bodian-Diamond syndrome ; Shwachman-Bodian-Diamond syndrome pseudogene	SBDS	155370	2
203965_at	ubiquitin specific peptidase 20	USP20	10868	2
227078_at	Musculoskeletal, embryonic nuclear protein 1	MGC52022	375346	2
206491_s_at	N-ethylmaleimide-sensitive factor attachment protein, alpha	NAPA	8775	2
1552283_s_at	zinc finger, DHHC-type containing 11	ZDHHC11	79844	2
205961_s_at	PC4 and SFRS1 interacting protein 1	PSIP1	11168	2
200948_at	myeloid leukemia factor 2	MLF2	8079	2
211358_s_at	CDKN1A interacting zinc finger protein 1	CIZ1	25792	2
202986_at	aryl-hydrocarbon receptor nuclear translocator 2	ARNT2	9915	2
201320_at	SWI/SNF related, matrix associated, actin dependent regulator of chromatin, subfamily c, member 2	SMARCC2	6601	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
238058_at	hypothetical protein LOC150381	LOC150381	150381	2
224301_x_at	H2A histone family, member J	H2AFJ	55766	2
226665_at	AHA1, activator of heat shock 90kDa protein ATPase homolog 2 (yeast)	AHSA2	130872	2
226839_at	TR4 orphan receptor associated protein TRA16	TRA16	126382	2
218502_s_at	trichorhinophalangeal syndrome I	TRPS1	7227	2
218326_s_at	leucine-rich repeat-containing G protein-coupled receptor 4	LGR4	55366	2
204432_at	SRY (sex determining region Y)-box 12	SOX12	6666	2
214043_at	Protein tyrosine phosphatase, receptor type, D	PTPRD	5789	2
212104_s_at	RNA binding motif protein 9	RBM9	23543	2
225019_at	calcium/calmodulin-dependent protein kinase (CaM kinase) II delta	CAMK2D	817	2
213107_at	TRAF2 and NCK interacting kinase	TNIK	23043	2
212878_s_at	kinesin 2	KNS2	3831	2
213493_at	sushi, nidogen and EGF-like domains 1	SNED1	25992	2
225191_at	cold inducible RNA binding protein	CIRBP	1153	2
218307_at	radical S-adenosyl methionine domain containing 1	RSAD1	55316	2
202417_at	kelch-like ECH-associated protein 1	KEAP1	9817	2
208748_s_at	flotillin 1	FLOT1	10211	2
204028_s_at	RAB GTPase activating protein 1	RABGAP1	23637	2
213012_at	neural precursor cell expressed, developmentally down-regulated 4	NEDD4	4734	2
1560060_s_at	vacuolar protein sorting 37C (yeast)	VPS37C	55048	2
217432_s_at	iduronate 2-sulfatase (Hunter syndrome)	IDS	3423	2
202939_at	zinc metallopeptidase (STE24 homolog, yeast)	ZMPSTE24	10269	2
225293_at	collagen, type XXVII, alpha 1	COL27A1	85301	2
1556059_s_at	spen homolog, transcriptional regulator (Drosophila)	SPEN	23013	2
204388_s_at	monoamine oxidase A	MAOA	4128	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
235562_at	hypothetical gene supported by AK091454	LOC285382	285382	2
233899_x_at	Zinc finger and BTB domain containing 10	ZBTB10	65986	2
219314_s_at	zinc finger protein 219	ZNF219	51222	2
208690_s_at	PDZ and LIM domain 1 (elfin)	PDLIM1	9124	2
208625_s_at	eukaryotic translation initiation factor 4 gamma, 1	EIF4G1	1981	2
1553994_at	5'-nucleotidase, ecto (CD73)	NT5E	4907	2
208814_at	Heat shock 70kDa protein 4	HSPA4	3308	2
214602_at	collagen, type IV, alpha 4	COL4A4	1286	2
1555789_s_at	PHD finger protein 23	PHF23	79142	2
228063_s_at	nucleosome assembly protein 1-like 5	NAP1L5	266812	2
216194_s_at	cytoskeleton associated protein 1	CKAP1	1155	2
222487_s_at	ribosomal protein S27-like	RPS27L	51065	2
209221_s_at	oxysterol binding protein-like 2	OSBPL2	9885	2
226288_s_at	neuroligin 2	NLGN2	57555	2
217890_s_at	parvin, alpha	PARVA	55742	2
226470_at	gamma-glutamyltransferase-like 3	GGTL3	2686	2
203956_at	MORC family CW-type zinc finger 2	MORC2	22880	2
223438_s_at	peroxisome proliferative activated receptor, alpha	PPARA	5465	2
227983_at	hypothetical protein MGC7036	MGC7036	196383	2
204270_at	v-ski sarcoma viral oncogene homolog (avian)	SKI	6497	2
205841_at	Janus kinase 2 (a protein tyrosine kinase)	JAK2	3717	2
200896_x_at	hepatoma-derived growth factor (high-mobility group protein 1-like)	HDGF	3068	2
214794_at	proliferation-associated 2G4, 38kDa	PA2G4	5036	2
212863_x_at	C-terminal binding protein 1	CTBP1	1487	2
203633_at	carnitine palmitoyltransferase 1A (liver)	CPT1A	1374	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
218215_s_at	nuclear receptor subfamily 1, group H, member 2	NR1H2	7376	2
203280_at	scaffold attachment factor B2	SAFB2	9667	2
213362_at	Protein tyrosine phosphatase, receptor type, D	PTPRD	5789	2
228725_x_at	HMT1 hnRNP methyltransferase-like 1 (S. cerevisiae)	HRMT1L1	3275	2
201602_s_at	protein phosphatase 1, regulatory (inhibitor) subunit 12A	PPP1R12A	4659	2
203836_s_at	mitogen-activated protein kinase kinase kinase 5	MAP3K5	4217	2
218504_at	fumarylacetoacetate hydrolase domain containing 2A	FAHD2A	51011	2
230027_s_at	mitochondrial ribosomal protein L43	MRPL43	84545	2
227155_at	LIM domain only 4	LMO4	8543	2
219046_s_at	PBX/knotted 1 homeobox 2	PKNOX2	63876	2
226075_at	splA/ryanodine receptor domain and SOCS box containing 1	SPSB1	80176	2
213278_at	myotubularin related protein 9	MTMR9	66036	2
204141_at	tubulin, beta 2	TUBB2	7280	2
203575_at	casein kinase 2, alpha prime polypeptide	CSNK2A2	1459	2
224743_at	inositol monophosphatase domain containing 1	IMPAD1	54928	2
211626_x_at	v-ets erythroblastosis virus E26 oncogene like (avian)	ERG	2078	2
202793_at	putative protein similar to nessy (Drosophila)	C3F	10162	2
203392_s_at	C-terminal binding protein 1	CTBP1	1487	2
203489_at	CD27-binding (Siva) protein	SIVA	10572	2
224661_at	phosphatidylinositol glycan class Y	PIG-Y	84992	2
225494_at	Dynein light chain 2	Dlc2	140735	2
225273_at	KIAA1280 protein	KIAA1280	55841	2
215707_s_at	prion protein (p27-30)	PRNP	5621	2
221256_s_at	haloacid dehalogenase-like hydrolase domain containing 3	HDHD3	81932	2
240983_s_at	cysteinyl-tRNA synthetase	CARS	833	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
216384_x_at	similar to prothymosin alpha	LOC440085	440085	2
216565_x_at	similar to Interferon-induced transmembrane protein 3 (Interferon-inducible protein 1-8U)	LOC391020	391020	2
202794_at	inositol polyphosphate-1-phosphatase	INPP1	3628	2
210465_s_at	small nuclear RNA activating complex, polypeptide 3, 50kDa	SNAPC3	6619	2
228855_at	similar to coenzyme A diphosphatase	LOC440388	440388	2
201661_s_at	acyl-CoA synthetase long-chain family member 3	ACSL3	2181	2
203909_at	solute carrier family 9 (sodium/hydrogen exchanger), member 6	SLC9A6	10479	2
208779_x_at	discoidin domain receptor family, member 1	DDR1	780	2
231726_at	protocadherin beta 14	PCDHB14	56122	2
209378_s_at	KIAA1128	KIAA1128	54462	2
201526_at	ADP-ribosylation factor 5	ARF5	381	2
1552426_a_at	TM2 domain containing 3	TM2D3	80213	2
202326_at	euchromatic histone-lysine N-methyltransferase 2	EHMT2	10919	2
224927_at	KIAA1949	KIAA1949	170954	2
239033_at	KIAA1958	KIAA1958	158405	2
221526_x_at	par-3 partitioning defective 3 homolog (C. elegans)	PARD3	56288	2
201482_at	quiescin Q6	QSCN6	5768	2
201491_at	AHA1, activator of heat shock 90kDa protein ATPase homolog 1 (yeast)	AHSA1	10598	2
218336_at	prefoldin 2	PFDN2	5202	2
218149_s_at	zinc finger protein 395	ZNF395	55893	2
242272_at	hypothetical protein FLJ32130	FLJ32130	146540	2
201021_s_at	destrin (actin depolymerizing factor)	DSTN	11034	2
216264_s_at	laminin, beta 2 (laminin S)	LAMB2	3913	2
223665_at	actin related protein M1	ARPM1	84517	2
210687_at	carnitine palmitoyltransferase 1A (liver)	CPT1A	1374	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201375_s_at	protein phosphatase 2 (formerly 2A), catalytic subunit, beta isoform	PPP2CB	5516	2
204021_s_at	purine-rich element binding protein A	PURA	5813	2
219114_at	chromosome 3 open reading frame 18	C3orf18	51161	2
230528_s_at	hypothetical protein MGC2752	MGC2752	65996	2
218994_s_at	stromal antigen 3-like	FLJ13195	64940	2
227265_at	MRNA; cDNA DKFZp686N07104 (from clone DKFZp686N07104)			2
217891_at	hypothetical protein FLJ13868	FLJ13868	64755	2
200932_s_at	dynactin 2 (p50)	DCTN2	10540	2
214071_at	Metallophosphoesterase 1	MPPE1	65258	2
220346_at	methylenetetrahydrofolate dehydrogenase (NADP+ dependent) 2-like	MTHFD2L	441024	2
1558924_s_at	restin (Reed-Steinberg cell-expressed intermediate filament-associated protein)	RSN	6249	2
201628_s_at	Ras-related GTP binding A	RRAGA	10670	2
211605_s_at	retinoic acid receptor, alpha ; retinoic acid receptor, alpha	RARA	5914	2
202022_at	aldolase C, fructose-bisphosphate	ALDOC	230	2
37022_at	proline/arginine-rich end leucine-rich repeat protein	PRELP	5549	2
206453_s_at	NDRG family member 2	NDRG2	57447	2
207124_s_at	guanine nucleotide binding protein (G protein), beta 5	GNB5	10681	2
212630_at	SEC6-like 1 (S. cerevisiae)	SEC6L1	11336	2
223519_at	sterile alpha motif and leucine zipper containing kinase AZK	ZAK	51776	2
214679_x_at	guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	2
207178_s_at	fyn-related kinase	FRK	2444	2
204032_at	breast cancer anti-estrogen resistance 3	BCAR3	8412	2
211793_s_at	abl interactor 2	ABI2	10152	2
228146_at	hypothetical protein LOC339263	LOC339263	339263	2
243017_at	Hypothetical protein LOC158572	LOC158572	158572	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
212791_at	hypothetical protein FLJ38984	FLJ38984	127703	2
201904_s_at	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase-like	CTDSPL	10217	2
234300_s_at	zinc finger protein 28 homolog (mouse)	ZFP28	140612	2
200852_x_at	guanine nucleotide binding protein (G protein), beta polypeptide 2	GNB2	2783	2
201651_s_at	protein kinase C and casein kinase substrate in neurons 2	PACSIN2	11252	2
218312_s_at	zinc finger protein 447	ZNF447	65982	2
223118_s_at	ubiquitin specific peptidase 47	USP47	55031	2
200622_x_at	calmodulin 3 (phosphorylase kinase, delta)	CALM3	808	2
201417_at	SRY (sex determining region Y)-box 4	SOX4	6659	2
230900_at	KM-HN-1 protein	KM-HN-1	256309	2
220864_s_at	NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 13	NDUFA13	51079	2
218601_at	up-regulated gene 4	URG4	55665	2
203120_at	tumor protein p53 binding protein, 2	TP53BP2	7159	2
235897_at	coatomer protein complex, subunit zeta 2	COPZ2	51226	2
236606_at	Salvador homolog 1 (Drosophila)	SAV1	60485	2
225404_at	hypothetical protein BC011880	LOC113444	113444	2
233955_x_at	CXXC finger 5	CXXC5	51523	2
200862_at	24-dehydrocholesterol reductase	DHCR24	1718	2
225442_at	Discoidin domain receptor family, member 2	DDR2	4921	2
224369_s_at	F-box protein 38 ; F-box protein 38	FBXO38	81545	2
227169_at	DnaJ (Hsp40) homolog, subfamily C, member 18	DNAJC18	202052	2
226996_at	lysocardiolipin acyltransferase	LYCAT	253558	2
219645_at	calsequestrin 1 (fast-twitch, skeletal muscle)	CASQ1	844	2
41160_at	methyl-CpG binding domain protein 3	MBD3	53615	2
236077_at	glucosidase, alpha; neutral C	GANC	2595	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
203035_s_at	protein inhibitor of activated STAT, 3	PIAS3	10401	2
201277_s_at	heterogeneous nuclear ribonucleoprotein A/B	HNRPAB	3182	2
201685_s_at	chromosome 14 open reading frame 92	C14orf92	9878	2
217981_s_at	fracture callus 1 homolog (rat)	FXC1	26515	2
201885_s_at	cytochrome b5 reductase 3	CYB5R3	1727	2
201469_s_at	SHC (Src homology 2 domain containing) transforming protein 1	SHC1	6464	2
213480_at	vesicle-associated membrane protein 4	VAMP4	8674	2
201282_at	oxoglutarate (alpha-ketoglutarate) dehydrogenase (lipoamide)	OGDH	4967	2
214107_x_at	hypothetical protein FLJ11822	LOC440434	440434	2
211009_s_at	zinc finger protein 271	ZNF271	10778	2
200721_s_at	ARP1 actin-related protein 1 homolog A, centractin alpha (yeast)	ACTR1A	10121	2
222493_s_at	testis expressed sequence 27	TEX27	60685	2
210102_at	loss of heterozygosity, 11, chromosomal region 2, gene A	LOH11CR2A	4013	2
218449_at	hypothetical protein FLJ11200	FLJ11200	55325	2
201790_s_at	7-dehydrocholesterol reductase	DHCR7	1717	2
206809_s_at	heterogeneous nuclear ribonucleoprotein A3	HNRPA3	220988	2
205139_s_at	uronyl-2-sulfotransferase	UST	10090	2
64899_at	lipid phosphate phosphatase-related protein type 2	LPPR2	64748	2
225086_at	Hypothetical protein FLJ38426	FLJ38426	283742	2
227481_at	CNKSR family member 3	CNKSR3	154043	2
213029_at	Nuclear factor I/B	NFIB	4781	2
221675_s_at	choline phosphotransferase 1	CHPT1	56994	2
1553961_s_at	chromosome 20 open reading frame 161	C20orf161	90203	2
218417_s_at	hypothetical protein FLJ20489	FLJ20489	55652	2
221506_s_at	transportin 2 (importin 3, karyopherin beta 2b)	TNPO2	30000	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
209041_s_at	ubiquitin-conjugating enzyme E2G 2 (UBC7 homolog, yeast)	UBE2G2	7327	2
200719_at	S-phase kinase-associated protein 1A (p19A)	SKP1A	6500	2
225914_s_at	calcium binding protein 39-like	CAB39L	81617	2
224516_s_at	CXXC finger 5 ; CXXC finger 5	CXXC5	51523	2
203150_at	Rab9 effector protein with kelch motifs	RABEPK	10244	2
31799_at	Coatomer protein complex, subunit beta 2 (beta prime)	COPB2	9276	2
239481_at	hypothetical protein FLJ37659	RP1-32F7.2	286499	2
203944_x_at	butyrophilin, subfamily 2, member A1	BTN2A1	11120	2
207076_s_at	argininosuccinate synthetase	ASS	445	2
210892_s_at	general transcription factor II, i	GTF2I	2969	2
32032_at	DiGeorge syndrome critical region gene 14	DGCR14	8220	2
242394_at	CNKSR family member 3	CNKSR3	154043	2
200609_s_at	WD repeat domain 1	WDR1	9948	2
222138_s_at	WD repeat domain 13	WDR13	64743	2
226604_at	SMILE protein	SMILE	160418	2
224634_at	G patch domain containing 4	GPATC4	54865	2
200634_at	profilin 1	PFN1	5216	2
202053_s_at	aldehyde dehydrogenase 3 family, member A2	ALDH3A2	224	2
203222_s_at	transducin-like enhancer of split 1 (E(sp1) homolog, Drosophila)	TLE1	7088	2
204038_s_at	endothelial differentiation, lysophosphatidic acid G-protein-coupled receptor, 2	EDG2	1902	2
225134_at	hypothetical protein FLJ14800	FLJ14800	84926	2
229873_at	hypothetical protein LOC283219	LOC283219	283219	2
219165_at	PDZ and LIM domain 2 (mystique)	PDLIM2	64236	2
215533_s_at	ubiquitination factor E4B (UFD2 homolog, yeast)	UBE4B	10277	2
209820_s_at	transducin (beta)-like 3	TBL3	10607	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
203467_at	phosphomannomutase 1	PMM1	5372	2
204012_s_at	leucine carboxyl methyltransferase 2	LCMT2	9836	2
236144_at	carboxypeptidase X (M14 family), member 2	CPXM2	119587	2
207480_s_at	Meis1, myeloid ecotropic viral integration site 1 homolog 2 (mouse)	MEIS2	4212	2
203244_at	peroxisomal biogenesis factor 5	PEX5	5830	2
229840_at	IQ motif and Sec7 domain 2	IQSEC2	23096	2
221710_x_at	chromosome 1 open reading frame 78 ; chromosome 1 open reading frame 78	C1orf78	55194	2
208735_s_at	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase 2	CTDSP2	10106	2
223174_at	BTB (POZ) domain containing 10	BTBD10	84280	2
1552548_at	Bartter syndrome, infantile, with sensorineural deafness (Barttin)	BSND	7809	2
235289_at	eukaryotic translation initiation factor 5A2	EIF5A2	56648	2
241813_at	methyl-CpG binding domain protein 1	MBD1	4152	2
209899_s_at	fuse-binding protein-interacting repressor	SIAHBP1	22827	2
226439_s_at	neurobeachin	NBEA	26960	2
209002_s_at	calcium binding and coiled-coil domain 1	CALCOCO1	57658	2
210460_s_at	proteasome (prosome, macropain) 26S subunit, non-ATPase, 4	PSMD4	5710	2
200824_at	glutathione S-transferase pi	GSTP1	2950	2
225766_s_at	Transportin 1	TNPO1	3842	2
212855_at	DCN1, defective in cullin neddylation 1, domain containing 4 (S. cerevisiae)	DCUN1D4	23142	2
232079_s_at	poliovirus receptor-related 2 (herpesvirus entry mediator B)	PVRL2	5819	2
218251_at	MID1 interacting protein 1 (gastrulation specific G12-like (zebrafish))	MID1IP1	58526	2
211985_s_at	calmodulin 1 (phosphorylase kinase, delta)	CALM1	801	2
227249_at	Myosin, heavy polypeptide 11, smooth muscle	MYH11	4629	2
219401_at	xylosyltransferase II	XYLT2	64132	2
238813_at	Aminolevulinate, delta-, synthase 2	ALAS2	212	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
223908_at	histone deacetylase 8	HDAC8	55869	2
209268_at	vacuolar protein sorting 45A (yeast)	VPS45A	11311	2
220014_at	mesenchymal stem cell protein DSC54	LOC51334	51334	2
203903_s_at	hephaestin	HEPH	9843	2
201168_x_at	Rho GDP dissociation inhibitor (GDI) alpha	ARHGDIA	396	2
202282_at	hydroxyacyl-Coenzyme A dehydrogenase, type II	HADH2	3028	2
212333_at	DKFZP564F0522 protein	DKFZP564F0522	25940	2
208928_at	P450 (cytochrome) oxidoreductase	POR	5447	2
223819_x_at	COMM domain containing 5	COMMD5	28991	2
211984_at	calmodulin 1 (phosphorylase kinase, delta)	CALM1	801	2
203781_at	mitochondrial ribosomal protein L33	MRPL33	9553	2
225454_at	hypothetical protein BC013949	LOC115098	115098	2
206649_s_at	transcription factor binding to IGHM enhancer 3	TFE3	7030	2
202439_s_at	iduronate 2-sulfatase (Hunter syndrome)	IDS	3423	2
235431_s_at	pellino homolog 3 (Drosophila)	PELI3	246330	2
1562059_at	Supervillin	SVIL	6840	2
210740_s_at	inositol 1,3,4-triphosphate 5/6 kinase	ITPK1	3705	2
219488_at	alpha 1,4-galactosyltransferase (globotriaosylceramide synthase)	A4GALT	53947	2
203373_at	suppressor of cytokine signaling 2	SOCS2	8835	2
234982_at	zinc finger protein 650	ZNF650	130507	2
226644_at	mindbomb homolog 2 (Drosophila)	MIB2	142678	2
228931_at	coenzyme Q4 homolog (yeast)	COQ4	51117	2
226195_at	MGC16028 similar to RIKEN cDNA 1700019E19 gene	MGC16028	112752	2
228433_at	hypothetical protein FLJ11236	FLJ11236	56008	2
204550_x_at	glutathione S-transferase M1	GSTM1	2944	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
202047_s_at	chromobox homolog 6	CBX6	23466	2
215171_s_at	translocase of inner mitochondrial membrane 17 homolog A (yeast)	TIMM17A	10440	2
227965_at	Adenomatosis polyposis coli 2	APC2	10297	2
214703_s_at	mannosidase, alpha, class 2B, member 2	MAN2B2	23324	2
221483_s_at	cyclic AMP phosphoprotein, 19 kD	ARPP-19	10776	2
218187_s_at	chromosome 8 open reading frame 33	C8orf33	65265	2
201557_at	vesicle-associated membrane protein 2 (synaptobrevin 2)	VAMP2	6844	2
202471_s_at	isocitrate dehydrogenase 3 (NAD+) gamma	IDH3G	3421	2
32811_at	myosin IC	MYO1C	4641	2
221519_at	F-box and WD-40 domain protein 4	FBXW4	6468	2
225278_at	protein kinase, AMP-activated, beta 2 non-catalytic subunit	PRKAB2	5565	2
242033_at	ring finger protein 180	RNF180	285671	2
227415_at	hypothetical protein LOC283508	LOC283508	283508	2
223743_s_at	mitochondrial ribosomal protein L4	MRPL4	51073	2
1559756_at	hypothetical protein DKFZp667F0711	DKFZp667F0711	399716	2
1553107_s_at	hypothetical protein FLJ37562	FLJ37562	134553	2
226102_at	Zinc finger protein 192	ZNF192	7745	2
200857_s_at	nuclear receptor co-repressor 1	NCOR1	9611	2
217770_at	phosphatidylinositol glycan, class T	PIGT	51604	2
223766_at	Clone FLB4246 PRO1102			2
238569_at	Gamma-aminobutyric acid (GABA) B receptor, 1	GABBR1	2550	2
59625_at	nucleolar protein 3 (apoptosis repressor with CARD domain)	NOL3	8996	2
213330_s_at	stress-induced-phosphoprotein 1 (Hsp70/Hsp90-organizing protein)	STIP1	10963	2
218773_s_at	methionine sulfoxide reductase B2	MSRB2	22921	2
217815_at	suppressor of Ty 16 homolog (S. cerevisiae)	SUPT16H	11198	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
227327_at	HBV pre-s2 binding protein 1	SBP1	90198	2
228402_at	zinc finger, BED-type containing 3	ZBED3	84327	2
209537_at	exostoses (multiple)-like 2	EXTL2	2135	2
229841_at	Eukaryotic translation initiation factor 2C, 2	EIF2C2	27161	2
218216_x_at	ADP-ribosylation-like factor 6 interacting protein 4	ARL6IP4	51329	2
203190_at	NADH dehydrogenase (ubiquinone) Fe-S protein 8, 23kDa (NADH-coenzyme Q reductase)	NDUFS8	4728	2
224662_at	kinesin family member 5B	KIF5B	3799	2
227170_at	Hypothetical protein DKFZp547K054	DKFZp547K054	56974	2
213383_at	SAPS domain family, member 2	KIAA0685	9701	2
225010_at	coiled-coil domain containing 6	CCDC6	8030	2
209513_s_at	hydroxysteroid dehydrogenase like 2	HSDL2	84263	2
223253_at	ependymin related protein 1 (zebrafish)	EPDR1	54749	2
208420_x_at	suppressor of Ty 6 homolog (S. cerevisiae)	SUPT6H	6830	2
223463_at	RAB23, member RAS oncogene family	RAB23	51715	2
226375_at	Lemur tyrosine kinase 2	LMTK2	22853	2
213310_at	Eukaryotic translation initiation factor 2C, 2	EIF2C2	27161	2
201121_s_at	progesterone receptor membrane component 1	PGRMC1	10857	2
205966_at	TAF13 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 18kDa	TAF13	6884	2
202378_s_at	leptin receptor overlapping transcript	LEPROT	54741	2
200649_at	nucleobindin 1	NUCB1	4924	2
212641_at	human immunodeficiency virus type I enhancer binding protein 2	HIVEP2	3097	2
225274_at	prenylcysteine oxidase 1	PCYOX1	51449	2
218367_x_at	ubiquitin specific peptidase 21	USP21	27005	2
227847_at	EPM2A (laforin) interacting protein 1	EPM2AIP1	9852	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
223604_at	GTPase activating Rap/RanGAP domain-like 3	GARNL3	84253	2
210612_s_at	synaptojanin 2	SYNJ2	8871	2
218262_at	hypothetical protein FLJ22318	FLJ22318	64777	2
214104_at	G protein-coupled receptor 161	GPR161	23432	2
235956_at	KIAA1377 protein	KIAA1377	57562	2
213684_s_at	PDZ and LIM domain 5	PDLIM5	10611	2
228778_at	Microcephaly, primary autosomal recessive 1	MCPH1	79648	2
218285_s_at	dehydrogenase/reductase (SDR family) member 6	DHRS6	56898	2
219940_s_at	hypothetical protein FLJ11305	FLJ11305	55795	2
201611_s_at	isoprenylcysteine carboxyl methyltransferase	ICMT	23463	2
200696_s_at	gelsolin (amyloidosis, Finnish type)	GSN	2934	2
209000_s_at	septin 8	Sep-08	23176	2
200613_at	adaptor-related protein complex 2, mu 1 subunit	AP2M1	1173	2
211928_at	dynein, cytoplasmic, heavy polypeptide 1	DNCH1	1778	2
202480_s_at	death effector domain containing	DEDD	9191	2
201544_x_at	poly(A) binding protein, nuclear 1	PABPN1	8106	2
227131_at	mitogen-activated protein kinase kinase kinase 3	MAP3K3	4215	2
236475_at	Microtubule associated monoxygenase, calponin and LIM domain containing 2	MICAL2	9645	2
219933_at	glutaredoxin 2	GLRX2	51022	2
227722_at	ribosomal protein S23	RPS23	6228	2
231738_at	protocadherin beta 7	PCDHB7	56129	2
208921_s_at	sorcin	SRI	6717	2
221434_s_at	chromosome 14 open reading frame 156 ; chromosome 14 open reading frame 156	C14orf156	81892	2
203771_s_at	biliverdin reductase A	BLVRA	644	2
200066_at	IK cytokine, down-regulator of HLA II ; IK cytokine, down-regulator of HLA II	IK	3550	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201906_s_at	CTD (carboxy-terminal domain, RNA polymerase II, polypeptide A) small phosphatase-like	CTDSPL	10217	2
227522_at	similar to mouse 2310016A09Rik gene	LOC134147	134147	2
201660_at	Acyl-CoA synthetase long-chain family member 3	ACSL3	2181	2
223119_s_at	ubiquitin specific peptidase 47	USP47	55031	2
1555360_a_at	DnaJ (Hsp40) homolog, subfamily C, member 11	DNAJC11	55735	2
229537_at	LIM domain only 4	LMO4	8543	2
203773_x_at	biliverdin reductase A	BLVRA	644	2
227181_at	hypothetical protein LOC348801	LOC348801	348801	2
201326_at	chaperonin containing TCP1, subunit 6A (zeta 1)	CCT6A	908	2
222093_s_at	zinc finger, HIT type 4	ZNHIT4	83444	2
208996_s_at	polymerase (RNA) II (DNA directed) polypeptide C, 33kDa	POLR2C	5432	2
200885_at	ras homolog gene family, member C	RHOC	389	2
209581_at	HRAS-like suppressor 3	HRASLS3	11145	2
222431_at	spindlin	SPIN	10927	2
212100_s_at	polymerase (DNA-directed), delta interacting protein 3	POLDIP3	84271	2
233881_s_at	toll interacting protein	TOLLIP	54472	2
1554429_a_at	dystrophia myotonica-containing WD repeat motif	DMWD	1762	2
1554147_s_at	chromosome 3 open reading frame 15	C3orf15	89876	2
207805_s_at	proteasome (prosome, macropain) 26S subunit, non-ATPase, 9	PSMD9	5715	2
209230_s_at	p8 protein (candidate of metastasis 1)	P8	26471	2
211271_x_at	polypyrimidine tract binding protein 1	PTBP1	5725	2
229176_at	Ankylosis, progressive homolog (mouse)	ANKH	56172	2
222011_s_at	t-complex 1	TCP1	6950	2
223006_s_at	chromosome 9 open reading frame 5	C9orf5	23731	2
202043_s_at	spermine synthase	SMS	6611	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
227127_at	Musculoskeletal, embryonic nuclear protein 1	MGC52022	375346	2
201536_at	dual specificity phosphatase 3 (vaccinia virus phosphatase VH1-related)	DUSP3	1845	2
214913_at	ADAM metallopeptidase with thrombospondin type 1 motif, 3	ADAMTS3	9508	2
237231_at	Chromosome 9 open reading frame 42	C9orf42	116224	2
227436_at	Zinc finger, A20 domain containing 1	ZA20D1	56957	2
200720_s_at	ARP1 actin-related protein 1 homolog A, centractin alpha (yeast)	ACTR1A	10121	2
201518_at	chromobox homolog 1 (HP1 beta homolog Drosophila)	CBX1	10951	2
233803_s_at	MYB binding protein (P160) 1a	MYBBP1A	10514	2
227959_at	Ankyrin repeat domain 9	ANKRD9	122416	2
224903_at	cirrhosis, autosomal recessive 1A (cirhin)	CIRH1A	84916	2
234001_s_at	ADP-ribosylation factor GTPase activating protein 1	ARFGAP1	55738	2
203258_at	DR1-associated protein 1 (negative cofactor 2 alpha)	DRAP1	10589	2
227477_at	zinc finger, MYND-type containing 19	ZMYND19	116225	2
209053_s_at	Wolf-Hirschhorn syndrome candidate 1	WHSC1	7468	2
210949_s_at	eukaryotic translation initiation factor 3, subunit 8, 110kDa	EIF3S8	8663	2
225531_at	Cdk5 and Abl enzyme substrate 1	CABLES1	91768	2
209972_s_at	JTV1 gene	JTV1	7965	2
218984_at	hypothetical protein FLJ20485	FLJ20485	54517	2
1563776_at	Hypothetical protein FLJ23342	FLJ23342	79684	2
203776_at	G patch domain and KOW motifs	GPKOW	27238	2
200642_at	superoxide dismutase 1, soluble (amyotrophic lateral sclerosis 1 (adult))	SOD1	6647	2
205353_s_at	prostatic binding protein	PBP	5037	2
234338_s_at	zinc finger protein 651	ZNF651	92999	2
201412_at	low density lipoprotein receptor-related protein 10	LRP10	26020	2
225753_at	zinc finger protein 513	ZNF513	130557	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201608_s_at	PWP1 homolog (S. cerevisiae)	PWP1	11137	2
201184_s_at	chromodomain helicase DNA binding protein 4	CHD4	1108	2
202058_s_at	karyopherin alpha 1 (importin alpha 5)	KPNA1	3836	2
214035_x_at	LOC399491 protein	LOC399491	399491	2
203186_s_at	S100 calcium binding protein A4 (calcium protein, calvasculin, metastasin, murine placental homolog)	S100A4	6275	2
226852_at	metastasis associated 1 family, member 3	MTA3	57504	2
213478_at	kazrin	KIAA1026	23254	2
212886_at	DKFZP434C171 protein	DKFZP434C171	26112	2
221489_s_at	sprouty homolog 4 (Drosophila)	SPRY4	81848	2
207721_x_at	histidine triad nucleotide binding protein 1	HINT1	3094	2
226776_at	enhancer of yellow 2 homolog (Drosophila)	ENY2	56943	2
222216_s_at	mitochondrial ribosomal protein L17	MRPL17	63875	2
211501_s_at	eukaryotic translation initiation factor 3, subunit 9 eta, 116kDa	EIF3S9	8662	2
212231_at	F-box protein 21	FBXO21	23014	2
212793_at	dishevelled associated activator of morphogenesis 2	DAAM2	23500	2
212206_s_at	H2A histone family, member V	H2AFV	94239	2
213660_s_at	topoisomerase (DNA) III beta	TOP3B	8940	2
1555881_s_at	leucine zipper, putative tumor suppressor 2	LZTS2	84445	2
226897_s_at	zinc finger CCCH-type containing 7A	ZC3H7A	29066	2
228019_s_at	mitochondrial ribosomal protein S18C	MRPS18C	51023	2
224636_at	zinc finger protein 91 homolog (mouse)	ZFP91	80829	2
210631_at	neurofibromin 1 (neurofibromatosis, von Recklinghausen disease, Watson disease)	NF1	4763	2
212017_at	hypothetical protein LOC130074	LOC130074	130074	2
209733_at	hypothetical protein LOC286440	LOC286440	286440	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
204464_s_at	endothelin receptor type A	EDNRA	1909	2
217914_at	two pore segment channel 1	TPCN1	53373	2
210002_at	GATA binding protein 6	GATA6	2627	2
200919_at	polyhomeotic-like 2 (Drosophila)	PHC2	1912	2
1561394_s_at	KIAA1755 protein	KIAA1755	85449	2
201405_s_at	COP9 constitutive photomorphogenic homolog subunit 6 (Arabidopsis)	COPS6	10980	2
213374_x_at	3-hydroxyisobutyryl-Coenzyme A hydrolase	HIBCH	26275	2
221598_s_at	cofactor required for Sp1 transcriptional activation, subunit 8, 34kDa	CRSP8	9442	2
208289_s_at	etoposide induced 2.4 mRNA	EI24	9538	2
1562228_s_at	phosphodiesterase 5A, cGMP-specific	PDE5A	8654	2
206274_s_at	ciliary rootlet coiled-coil, rootletin	CROCC	9696	2
231876_at	tripartite motif-containing 56	TRIM56	81844	2
212711_at	calmodulin regulated spectrin-associated protein 1	CAMSAP1	157922	2
226692_at	Small EDRK-rich factor 2	SERF2	10169	2
213473_at	BRCA1 associated protein	BRAP	8315	2
225376_at	chromosome 20 open reading frame 11	C20orf11	54994	2
1552705_at	dual specificity phosphatase 19	DUSP19	142679	2
218472_s_at	pelota homolog (Drosophila)	PELO	53918	2
201864_at	GDP dissociation inhibitor 1	GDI1	2664	2
227256_at	ubiquitin specific peptidase 31	USP31	57478	2
203636_at	midline 1 (Opitz/BBB syndrome)	MID1	4281	2
635_s_at	protein phosphatase 2, regulatory subunit B (B56), beta isoform	PPP2R5B	5526	2
219637_at	armadillo repeat containing 9	ARMC9	80210	2
209882_at	Ras-like without CAAX 1	RIT1	6016	2
218488_at	eukaryotic translation initiation factor 2B, subunit 3 gamma, 58kDa	EIF2B3	8891	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
209667_at	carboxylesterase 2 (intestine, liver)	CES2	8824	2
201142_at	eukaryotic translation initiation factor 2, subunit 1 alpha, 35kDa	EIF2S1	1965	2
223446_s_at	dystrobrevin binding protein 1	DTNBP1	84062	2
241866_at	solute carrier family 16 (monocarboxylic acid transporters), member 7	SLC16A7	9194	2
201226_at	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 8, 19kDa	NDUFB8	4714	2
224522_s_at	hypothetical protein FLJ22955 ; hypothetical protein FLJ22955	FLJ22955	79877	2
1552295_a_at	solute carrier family 39 (zinc transporter), member 13	SLC39A13	91252	2
202116_at	D4, zinc and double PHD fingers family 2	DPF2	5977	2
213269_at	zinc finger protein 248	ZNF248	57209	2
212509_s_at	matrix-remodelling associated 7	MXRA7	439921	2
203208_s_at	mitochondrial fission regulator 1	MTFR1	9650	2
202839_s_at	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 7, 18kDa	NDUFB7	4713	2
228950_s_at	chromosome 1 open reading frame 139	C1orf139	79971	2
223130_s_at	myosin regulatory light chain interacting protein	MYLIP	29116	2
226246_at	potassium channel tetramerisation domain containing 1	KCTD1	284252	2
225953_at	hypothetical protein FLJ10656	P15RS	55197	2
224013_s_at	SRY (sex determining region Y)-box 7	SOX7	83595	2
224632_at	G patch domain containing 4	GPATC4	54865	2
221693_s_at	mitochondrial ribosomal protein S18A ; mitochondrial ribosomal protein S18A	MRPS18A	55168	2
229838_at	nucleobindin 2	NUCB2	4925	2
210880_s_at	embryonal Fyn-associated substrate	EFS	10278	2
216863_s_at	MORC family CW-type zinc finger 2	MORC2	22880	2
217830_s_at	NSFL1 (p97) cofactor (p47)	NSFL1C	55968	2
201851_at	SH3-domain GRB2-like 1	SH3GL1	6455	2
218183_at	chromosome 16 open reading frame 5	C16orf5	29965	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
212662_at	poliovirus receptor	PVR	5817	2
214306_at	optic atrophy 1 (autosomal dominant)	OPA1	4976	2
223110_at	KIAA1429	KIAA1429	25962	2
226784_at	TWIST neighbor	TWISTNB	221830	2
226015_at	zinc finger protein 12	ZNF12	7559	2
40016_g_at	microtubule associated serine/threonine kinase family member 4	MAST4	23227	2
236273_at	hypothetical protein FLJ20719	FLJ20719	55672	2
200683_s_at	ubiquitin-conjugating enzyme E2L 3	UBE2L3	7332	2
200785_s_at	low density lipoprotein-related protein 1 (alpha-2-macroglobulin receptor)	LRP1	4035	2
201276_at	RAB5B, member RAS oncogene family	RAB5B	5869	2
212955_s_at	polymerase (RNA) II (DNA directed) polypeptide I, 14.5kDa	POLR2I	5438	2
209178_at	DEAH (Asp-Glu-Ala-His) box polypeptide 38	DHX38	9785	2
218664_at	mitochondrial trans-2-enoyl-CoA reductase	MECR	51102	2
204928_s_at	solute carrier family 10 (sodium/bile acid cotransporter family), member 3	SLC10A3	8273	2
228977_at	Interleukin 17D	IL17D	53342	2
224823_at	myosin, light polypeptide kinase	MYLK	4638	2
201350_at	flotillin 2	FLOT2	2319	2
225481_at	FERM domain containing 6	FRMD6	122786	2
205545_x_at	DnaJ (Hsp40) homolog, subfamily C, member 8	DNAJC8	22826	2
221480_at	heterogeneous nuclear ribonucleoprotein D (AU-rich element RNA binding protein 1, 37kDa)	HNRPD	3184	2
212055_at	chromosome 18 open reading frame 10	C18orf10	25941	2
228630_at	Zinc finger protein 84 (HPF2)	ZNF84	7637	2
209352_s_at	SIN3 homolog B, transcription regulator (yeast)	SIN3B	23309	2
229394_s_at	Glucocorticoid receptor DNA binding factor 1	GRLF1	2909	2
216620_s_at	Rho guanine nucleotide exchange factor (GEF) 10	ARHGEF10	9639	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
212148_at	Pre-B-cell leukemia transcription factor 1	PBX1	5087	2
230657_at	Clock homolog (mouse)	CLOCK	9575	2
1557578_at	Pleckstrin homology-like domain, family B, member 2	PHLDB2	90102	2
1553960_at	chromosome 20 open reading frame 161	C20orf161	90203	2
227976_at	alpha-2-macroglobulin	A2M	2	2
228155_at	chromosome 10 open reading frame 58	C10orf58	84293	2
213122_at	TSPY-like 5	TSPYL5	85453	2
217841_s_at	protein phosphatase methylesterase-1	PME-1	51400	2
209009_at	esterase D/formylglutathione hydrolase	ESD	2098	2
219203_at	chromosome 14 open reading frame 122	C14orf122	51016	2
201043_s_at	acidic (leucine-rich) nuclear phosphoprotein 32 family, member A	ANP32A	8125	2
221771_s_at	M-phase phosphoprotein, mpp8	HSMPP8	54737	2
202172_at	zinc finger protein 161	ZNF161	7716	2
212453_at	KIAA1279	KIAA1279	26128	2
212217_at	prolyl endopeptidase-like	PREPL	9581	2
213318_s_at	HLA-B associated transcript 3	BAT3	7917	2
204355_at	DEAH (Asp-Glu-Ala-His) box polypeptide 30	DHX30	22907	2
203271_s_at	unc-119 homolog (C. elegans)	UNC119	9094	2
201946_s_at	chaperonin containing TCP1, subunit 2 (beta)	CCT2	10576	2
228073_at	haloacid dehalogenase-like hydrolase domain containing 4	HDHD4	140838	2
229344_x_at	family with sequence similarity 80, member B	FAM80B	57494	2
226331_at	Bobby sox homolog (Drosophila)	BBX	56987	2
201831_s_at	vesicle docking protein p115	VDP	8615	2
235405_at	glutathione S-transferase A4	GSTA4	2941	2
225900_at	SEC15-like 2 (S. cerevisiae)	SEC15L2	23233	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
219142_at	RAS-like, family 11, member B	RASL11B	65997	2
227188_at	chromosome 21 open reading frame 63	C21orf63	59271	2
228098_s_at	myosin regulatory light chain interacting protein	MYLIP	29116	2
202773_s_at	splicing factor, arginine/serine-rich 8 (suppressor-of-white-apricot homolog, Drosophila)	SFRS8	6433	2
231213_at	phosphodiesterase 1A, calmodulin-dependent	PDE1A	5136	2
224576_at	endoplasmic reticulum-golgi intermediate compartment 32 kDa protein	KIAA1181	57222	2
239415_at	ASAP	FLJ21159	79884	2
223081_at	PHD finger protein 23	PHF23	79142	2
238556_at	Calcium/calmodulin-dependent protein kinase (CaM kinase) II gamma	CAMK2G	818	2
214359_s_at	heat shock 90kDa protein 1, beta	HSPCB	3326	2
201980_s_at	Ras suppressor protein 1	RSU1	6251	2
223132_s_at	tripartite motif-containing 8	TRIM8	81603	2
226081_at	Leucine zipper and CTNNBIP1 domain containing	LZIC	84328	2
201673_s_at	glycogen synthase 1 (muscle)	GYS1	2997	2
219346_at	leucine rich repeat and fibronectin type III domain containing 3	LRFN3	79414	2
1554480_a_at	SVH protein	SVH	83787	2
206818_s_at	cyclin M2	CNNM2	54805	2
234284_at	guanine nucleotide binding protein (G protein), gamma 8	GNG8	94235	2
226701_at	gap junction protein, alpha 5, 40kDa (connexin 40)	GJA5	2702	2
212508_at	modulator of apoptosis 1	MOAP1	64112	2
200770_s_at	laminin, gamma 1 (formerly LAMB2)	LAMC1	3915	2
201259_s_at	synaptophysin-like 1	SYPL1	6856	2
223093_at	ankylosis, progressive homolog (mouse)	ANKH	56172	2
201871_s_at	unknown protein LOC51035	LOC51035	51035	2
202104_s_at	spastic paraplegia 7, paraplegin (pure and complicated autosomal recessive)	SPG7	6687	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
227557_at	scavenger receptor class F, member 2	SCARF2	91179	2
31874_at	growth arrest-specific 2 like 1	GAS2L1	10634	2
206200_s_at	annexin A11	ANXA11	311	2
221939_at	Yip1 domain family, member 2	YIPF2	78992	2
207428_x_at	cell division cycle 2-like 1 (PITSLRE proteins) ; cell division cycle 2-like 2 (PITSLRE proteins)	CDC2L1 ; CDC2L2	984 ; 985	2
221942_s_at	guanylate cyclase 1, soluble, alpha 3	GUCY1A3	2982	2
228006_at	Phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	PTEN	5728	2
230353_at	hypothetical protein LOC284112	LOC284112	284112	2
203267_s_at	developmentally regulated GTP binding protein 2	DRG2	1819	2
1566257_at	Hypothetical protein LOC144874	LOC144874	144874	2
209019_s_at	PTEN induced putative kinase 1	PINK1	65018	2
203885_at	RAB21, member RAS oncogene family	RAB21	23011	2
226010_at	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 23	SLC25A23	79085	2
204090_at	serine/threonine kinase 19	STK19	8859	2
203822_s_at	E74-like factor 2 (ets domain transcription factor)	ELF2	1998	2
231945_at	filamin A interacting protein 1	FILIP1	27145	2
209511_at	polymerase (RNA) II (DNA directed) polypeptide F	POLR2F	5435	2
218034_at	tetratricopeptide repeat domain 11	TTC11	51024	2
40687_at	gap junction protein, alpha 4, 37kDa (connexin 37)	GJA4	2701	2
202019_s_at	LanC lantibiotic synthetase component C-like 1 (bacterial)	LANCL1	10314	2
213617_s_at	chromosome 18 open reading frame 10	C18orf10	25941	2
203562_at	fasciculation and elongation protein zeta 1 (zygin I)	FEZ1	9638	2
212979_s_at	KIAA0738 gene product	KIAA0738	9747	2
226241_s_at	mitochondrial ribosomal protein L52	MRPL52	122704	2
201425_at	aldehyde dehydrogenase 2 family (mitochondrial)	ALDH2	217	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
1570511_at	Rho guanine nucleotide exchange factor (GEF) 10-like	ARHGEF10L	55160	2
202759_s_at	PALM2-AKAP2 protein	PALM2-AKAP2	445815	2
221641_s_at	acyl-CoA thioesterase 9	ACOT9	23597	2
205168_at	discoidin domain receptor family, member 2	DDR2	4921	2
218116_at	chromosome 9 open reading frame 78 ; chromosome 9 open reading frame 78	C9orf78	51759	2
201419_at	BRCA1 associated protein-1 (ubiquitin carboxy-terminal hydrolase)	BAP1	8314	2
225206_s_at	Similar to mitochondrial translational release factor 1-like	MTRF1L	54516	2
224838_at	forkhead box P1	FOXP1	27086	2
228856_at	Hypothetical protein MGC2474	MGC2474	65988	2
210825_s_at	prostatic binding protein	PBP	5037	2
204068_at	serine/threonine kinase 3 (STE20 homolog, yeast)	STK3	6788	2
33307_at	CGI-96 protein	CGI-96	27341	2
203032_s_at	fumarate hydratase	FH	2271	2
218516_s_at	inositol monophosphatase domain containing 1	IMPAD1	54928	2
212098_at	hypothetical protein LOC151162	LOC151162	151162	2
226967_at	hypothetical protein FLJ14768	FLJ14768	84922	2
224616_at	dynein, cytoplasmic, light intermediate polypeptide 2	DNCLI2	1783	2
212215_at	prolyl endopeptidase-like	PREPL	9581	2
218297_at	chromosome 10 open reading frame 97	C10orf97	80013	2
238154_at	P10-binding protein	Cep70	80321	2
224945_at	BTB (POZ) domain containing 7	BTBD7	55727	2
242443_at	Echinoderm microtubule associated protein like 5	EML5	161436	2
227150_at	Metal-regulatory transcription factor 1	MTF1	4520	2
203727_at	superkiller viralicidic activity 2-like (S. cerevisiae)	SKIV2L	6499	2
225200_at	zinc finger, CSL-type containing 2	ZCSL2	285381	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
222206_s_at	nicalin homolog (zebrafish)	NCLN	56926	2
226761_at	zinc finger protein, subfamily 1A, 4 (Eos)	ZNFN1A4	64375	2
210762_s_at	deleted in liver cancer 1	DLC1	10395	2
202045_s_at	glucocorticoid receptor DNA binding factor 1	GRLF1	2909	2
203864_s_at	actinin, alpha 2	ACTN2	88	2
226050_at	transmembrane and coiled-coil domains 3	TMCO3	55002	2
200694_s_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 24	DDX24	57062	2
202226_s_at	v-crk sarcoma virus CT10 oncogene homolog (avian)	CRK	1398	2
225793_at	Lix1 homolog (mouse) like	LIX1L	128077	2
213249_at	F-box and leucine-rich repeat protein 7	FBXL7	23194	2
1555730_a_at	cofilin 1 (non-muscle)	CFL1	1072	2
202732_at	protein kinase (cAMP-dependent, catalytic) inhibitor gamma	PKIG	11142	2
208962_s_at	fatty acid desaturase 1	FADS1	3992	2
213306_at	multiple PDZ domain protein	MPDZ	8777	2
218020_s_at	testis expressed sequence 27	TEX27	60685	2
201440_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 23	DDX23	9416	2
200734_s_at	ADP-ribosylation factor 3	ARF3	377	2
218522_s_at	BPY2 interacting protein 1	BPY2IP1	55201	2
218572_at	chromatin modifying protein 4A	CHMP4A	29082	2
226000_at	CTTNBP2 N-terminal like	DKFZp547A023	55917	2
232146_at	NADH dehydrogenase (ubiquinone) 1, subcomplex unknown, 1, 6kDa	NDUFC1	4717	2
220841_s_at	Abelson helper integration site	AHI1	54806	2
45749_at	family with sequence similarity 65, member A	FAM65A	79567	2
201380_at	cartilage associated protein	CRTAP	10491	2
219532_at	elongation of very long chain fatty acids (FEN1/Elo2, SUR4/Elo3, yeast)-like 4	ELOVL4	6785	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
221570_s_at	methyltransferase like 5	METTL5	29081	2
201420_s_at	WD repeat domain 77	WDR77	79084	2
202470_s_at	cleavage and polyadenylation specific factor 6, 68kDa	CPSF6	11052	2
225110_at	hypothetical protein FLJ10826	FLJ10826	55239	2
202985_s_at	BCL2-associated athanogene 5	BAG5	9529	2
202461_at	eukaryotic translation initiation factor 2B, subunit 2 beta, 39kDa	EIF2B2	8892	2
229595_at	coiled-coil-helix-coiled-coil-helix domain containing 4	CHCHD4	131474	2
204676_at	chromosome 16 open reading frame 51	C16orf51	25880	2
212396_s_at	KIAA0090	KIAA0090	23065	2
238688_at	Tropomyosin 1 (alpha)	TPM1	7168	2
207088_s_at	solute carrier family 25 (mitochondrial carrier; oxoglutarate carrier), member 11	SLC25A11	8402	2
222171_s_at	PBX/knotted 1 homeobox 2	PKNOX2	63876	2
212103_at	Karyopherin alpha 6 (importin alpha 7)	KPNA6	23633	2
218111_s_at	cytidine monophosphate N-acetylneuraminic acid synthetase	CMAS	55907	2
215185_at	hypothetical gene supported by AK024177	LOC441468	441468	2
204577_s_at	clusterin associated protein 1	CLUAP1	23059	2
1556764_s_at	Phosphodiesterase 4D, cAMP-specific (phosphodiesterase E3 dunce homolog, Drosophila)	PDE4D	5144	2
243948_at	Echinoderm microtubule associated protein like 5	EML5	161436	2
220230_s_at	cytochrome b5 reductase 2	CYB5R2	51700	2
203866_at	notchless homolog 1 (Drosophila)	NLE1	54475	2
229732_at	ZFP-36 for a zinc finger protein	HSZFP36	55552	2
228062_at	nucleosome assembly protein 1-like 5	NAP1L5	266812	2
228445_at	apoptosis-inducing factor (AIF)-like mitochondrion-associated inducer of death	AMID	84883	2
210418_s_at	isocitrate dehydrogenase 3 (NAD+) beta	IDH3B	3420	2
202212_at	pescadillo homolog 1, containing BRCT domain (zebrafish)	PES1	23481	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
218224_at	paraneoplastic antigen MA1	PNMA1	9240	2
217902_s_at	hect domain and RLD 2	HERC2	8924	2
203515_s_at	phosphomevalonate kinase	PMVK	10654	2
201153_s_at	muscleblind-like (Drosophila)	MBNL1	4154	2
202102_s_at	bromodomain containing 4	BRD4	23476	2
1559954_s_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 42	DDX42	11325	2
212025_s_at	flightless I homolog (Drosophila)	FLII	2314	2
200995_at	Importin 7	IPO7	10527	2
210896_s_at	aspartate beta-hydroxylase	ASPH	444	2
226402_at	cytochrome P450, family 2, subfamily U, polypeptide 1	CYP2U1	113612	2
213191_at	toll-like receptor adaptor molecule 1	TICAM1	148022	2
225359_at	DnaJ (Hsp40) homolog, subfamily C, member 19	DNAJC19	131118	2
202919_at	preimplantation protein 3	PREI3	25843	2
212904_at	leucine rich repeat containing 47	LRRC47	57470	2
226978_at	peroxisome proliferative activated receptor, alpha	PPARA	5465	2
203252_at	CDK2-associated protein 2	CDK2AP2	10263	2
224994_at	calcium/calmodulin-dependent protein kinase (CaM kinase) II delta	CAMK2D	817	2
225406_at	twisted gastrulation homolog 1 (Drosophila)	TWSG1	57045	2
214999_s_at	RAB11 family interacting protein 3 (class II)	RAB11FIP3	9727	2
202721_s_at	glutamine-fructose-6-phosphate transaminase 1	GFPT1	2673	2
202387_at	BCL2-associated athanogene ; BCL2-associated athanogene	BAG1	573	2
203692_s_at	E2F transcription factor 3	E2F3	1871	2
201379_s_at	tumor protein D52-like 2	TPD52L2	7165	2
212458_at	sprouty-related, EVH1 domain containing 2	SPRED2	200734	2
227980_at	HLA complex group 12	HCG12	493826	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
200955_at	inner membrane protein, mitochondrial (mitofilin)	IMMT	10989	2
200974_at	actin, alpha 2, smooth muscle, aorta	ACTA2	59	2
221732_at	calcium activated nucleotidase 1	CANT1	124583	2
236648_at	Guanine monphosphate synthetase	GMPS	8833	2
205547_s_at	transgelin	TAGLN	6876	2
225692_at	calmodulin binding transcription activator 1	CAMTA1	23261	2
55065_at	MAP/microtubule affinity-regulating kinase 4	MARK4	57787	2
203261_at	dynactin 6	DCTN6	10671	2
224561_s_at	mortality factor 4 like 1	MORF4L1	10933	2
209503_s_at	proteasome (prosome, macropain) 26S subunit, ATPase, 5	PSMC5	5705	2
225521_at	anaphase promoting complex subunit 7	ANAPC7	51434	2
201263_at	threonyl-tRNA synthetase	TARS	6897	2
200637_s_at	protein tyrosine phosphatase, receptor type, F	PTPRF	5792	2
202119_s_at	copine III	CPNE3	8895	2
222212_s_at	LAG1 longevity assurance homolog 2 (S. cerevisiae)	LASS2	29956	2
204963_at	sarcospan (Kras oncogene-associated gene)	SSPN	8082	2
200647_x_at	eukaryotic translation initiation factor 3, subunit 8, 110kDa	EIF3S8	8663	2
223178_s_at	5'-nucleotidase, cytosolic II-like 1	NT5C2L1	221294	2
222883_at	chromosome 1 open reading frame 163	C1orf163	65260	2
203462_x_at	eukaryotic translation initiation factor 3, subunit 9 eta, 116kDa	EIF3S9	8662	2
218938_at	F-box and leucine-rich repeat protein 15	FBXL15	79176	2
218648_at	transducer of regulated cAMP response element-binding protein (CREB) 3	TORC3	64784	2
202695_s_at	serine/threonine kinase 17a (apoptosis-inducing)	STK17A	9263	2
203458_at	sepiapterin reductase (7,8-dihydrobiopterin:NADP+ oxidoreductase)	SPR	6697	2
226002_at	GRB2-associated binding protein 1	GAB1	2549	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
213230_at	paraneoplastic antigen	HUMPPA	30850	2
222504_s_at	COX4 neighbor	COX4NB	10328	2
209608_s_at	acetyl-Coenzyme A acetyltransferase 2 (acetoacetyl Coenzyme A thiolase)	ACAT2	39	2
226592_at	Hypothetical protein LOC286334	LOC286334	286334	2
213766_x_at	guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	2
226813_at	Chromosome 1 open reading frame 57	MGC13186	84284	2
225731_at	KIAA1223 protein	KIAA1223	57182	2
208678_at	ATPase, H+ transporting, lysosomal 31kDa, V1 subunit E isoform 1	ATP6V1E1	529	2
223099_s_at	peroxisomal LON protease like	LONPL	83752	2
214484_s_at	opioid receptor, sigma 1	OPRS1	10280	2
207645_s_at	chromodomain helicase DNA binding protein 1-like	CHD1L	9557	2
231086_at	Beta-site APP-cleaving enzyme 1	BACE1	23621	2
217140_s_at	voltage-dependent anion channel 1	VDAC1	7416	2
225492_at	CCR4-NOT transcription complex, subunit 3	CNOT3	4849	2
203239_s_at	Bobby sox homolog (Drosophila)	BBX	56987	2
202914_s_at	Rho guanine nucleotide exchange factor (GEF) 11	ARHGEF11	9826	2
200064_at	heat shock 90kDa protein 1, beta ; heat shock 90kDa protein 1, beta	HSPCB	3326	2
223437_at	peroxisome proliferative activated receptor, alpha	PPARA	5465	2
223909_s_at	histone deacetylase 8	HDAC8	55869	2
229265_at	Atrophin 1	DRPLA	1822	2
218816_at	leucine rich repeat containing 1	LRRC1	55227	2
209155_s_at	5'-nucleotidase, cytosolic II	NT5C2	22978	2
201152_s_at	muscleblind-like (Drosophila)	MBNL1	4154	2
201478_s_at	dyskeratosis congenita 1, dyskerin	DKC1	1736	2
224808_s_at	chromosome 7 open reading frame 20	C7orf20	51608	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
206953_s_at	latrophilin 2	LPHN2	23266	2
211952_at	RAN binding protein 5	RANBP5	3843	2
206388_at	phosphodiesterase 3A, cGMP-inhibited	PDE3A	5139	2
208660_at	citrate synthase	CS	1431	2
219737_s_at	protocadherin 9	PCDH9	5101	2
223424_s_at	zinc finger protein 38	ZNF38	7589	2
1557073_s_at	Tau tubulin kinase 2	TTBK2	146057	2
203423_at	retinol binding protein 1, cellular	RBP1	5947	2
201199_s_at	proteasome (prosome, macropain) 26S subunit, non-ATPase, 1	PSMD1	5707	2
223147_s_at	WD repeat domain 33	WDR33	55339	2
210011_s_at	Ewing sarcoma breakpoint region 1	EWSR1	2130	2
37201_at	inter-alpha (globulin) inhibitor H4 (plasma Kallikrein-sensitive glycoprotein)	ITIH4	3700	2
224729_s_at	ATP synthase mitochondrial F1 complex assembly factor 1	ATPAF1	64756	2
205672_at	xeroderma pigmentosum, complementation group A	XPA	7507	2
36553_at	acetylserotonin O-methyltransferase-like	ASMTL	8623	2
219244_s_at	mitochondrial ribosomal protein L46	MRPL46	26589	2
205665_at	tetraspanin 9	TSPAN9	10867	2
243816_at	Zinc finger protein 70 (Cos17)	ZNF70	7621	2
241206_at	Alpha-2-macroglobulin	A2M	2	2
221588_x_at	aldehyde dehydrogenase 6 family, member A1	ALDH6A1	4329	2
240928_at	Chromosome 14 open reading frame 111	C14orf111	51077	2
201059_at	cortactin	CTTN	2017	2
217842_at	LUC7-like 2 (S. cerevisiae)	LUC7L2	51631	2
202361_at	SEC24 related gene family, member C (S. cerevisiae)	SEC24C	9632	2
225853_at	glucosamine-phosphate N-acetyltransferase 1	GNPNAT1	64841	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
1554867_a_at	mesenchymal stem cell protein DSC54	LOC51334	51334	2
201056_at	Golgi autoantigen, golgin subfamily b, macrogolgin (with transmembrane signal), 1	GOLGB1	2804	2
218086_at	neural proliferation, differentiation and control, 1	NPDC1	56654	2
221606_s_at	nucleosomal binding protein 1	NSBP1	79366	2
226896_at	coiled-coil-helix-coiled-coil-helix domain containing 1	CHCHD1	118487	2
212102_s_at	karyopherin alpha 6 (importin alpha 7)	KPNA6	23633	2
230274_s_at	Rabaptin, RAB GTPase binding effector protein 1	RABEP1	9135	2
201636_at	fragile X mental retardation, autosomal homolog 1	FXR1	8087	2
217917_s_at	dynein, cytoplasmic, light polypeptide 2A	DNCL2A	83658	2
206050_s_at	ribonuclease/angiogenin inhibitor 1	RNH1	6050	2
32402_s_at	symplekin	SYMPK	8189	2
205803_s_at	transient receptor potential cation channel, subfamily C, member 1	TRPC1	7220	2
201327_s_at	chaperonin containing TCP1, subunit 6A (zeta 1)	CCT6A	908	2
205516_x_at	CDKN1A interacting zinc finger protein 1	CIZ1	25792	2
201138_s_at	Sjogren syndrome antigen B (autoantigen La)	SSB	6741	2
233082_at	zinc finger protein 630	ZNF630	57232	2
225144_at	bone morphogenetic protein receptor, type II (serine/threonine kinase)	BMPR2	659	2
222737_s_at	bromodomain containing 7	BRD7	29117	2
216976_s_at	RYK receptor-like tyrosine kinase	RYK	6259	2
203529_at	protein phosphatase 6, catalytic subunit	PPP6C	5537	2
223328_at	SVH protein	SVH	83787	2
203724_s_at	rap2 interacting protein x	RIPX	22902	2
213272_s_at	promethin	LOC57146	57146	2
220293_at	chromosome 14 open reading frame 161	C14orf161	79820	2
225252_at	sulfiredoxin 1 homolog (S. cerevisiae)	SRXN1	140809	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
202125_s_at	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 3	ALS2CR3	66008	2
226090_x_at	RAB, member of RAS oncogene family-like 3	RABL3	285282	2
200635_s_at	protein tyrosine phosphatase, receptor type, F	PTPRF	5792	2
217776_at	retinol dehydrogenase 11 (all-trans and 9-cis)	RDH11	51109	2
203119_at	hypothetical protein MGC2574	MGC2574	79080	2
212818_s_at	ankyrin repeat and SOCS box-containing 1	ASB1	51665	2
41113_at	zinc finger protein 500	ZNF500	26048	2
202415_s_at	hsp70-interacting protein	HSPBP1	23640	2
225118_at	PR/SET domain containing protein 8	SET8	387893	2
203192_at	ATP-binding cassette, sub-family B (MDR/TAP), member 6	ABCB6	10058	2
231765_at	zinc finger, FYVE domain containing 20	ZFYVE20	64145	2
218415_at	vacuolar protein sorting 33B (yeast)	VPS33B	26276	2
1565830_at	KIAA1731	KIAA1731	85459	2
1554555_a_at	hypothetical protein FLJ21148	FLJ21148	79918	2
214736_s_at	adducin 1 (alpha)	ADD1	118	2
200758_s_at	nuclear factor (erythroid-derived 2)-like 1	NFE2L1	4779	2
205066_s_at	ectonucleotide pyrophosphatase/phosphodiesterase 1	ENPP1	5167	2
224928_at	SET domain-containing protein 7	SET7	80854	2
227587_at	hypothetical protein FLJ12949	FLJ12949	65095	2
205008_s_at	calcium and integrin binding family member 2	CIB2	10518	2
203837_at	mitogen-activated protein kinase kinase kinase 5	MAP3K5	4217	2
223240_at	F-box protein 8	FBXO8	26269	2
209316_s_at	HBS1-like (S. cerevisiae)	HBS1L	10767	2
219188_s_at	LRP16 protein	LRP16	28992	2
235195_at	F-box and WD-40 domain protein 2	FBXW2	26190	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
218377_s_at	chromosome 21 open reading frame 6	C21orf6	10069	2
222841_s_at	translocase of inner mitochondrial membrane 22 homolog (yeast)	TIMM22	29928	2
212076_at	myeloid/lymphoid or mixed-lineage leukemia (trithorax homolog, Drosophila)	MLL	4297	2
200816_s_at	platelet-activating factor acetylhydrolase, isoform Ib, alpha subunit 45kDa	PAFAH1B1	5048	2
221813_at	F-box protein 42	FBXO42	54455	2
200876_s_at	proteasome (prosome, macropain) subunit, beta type, 1	PSMB1	5689	2
217737_x_at	chromosome 20 open reading frame 43	C20orf43	51507	2
238719_at	Protein phosphatase 2 (formerly 2A), catalytic subunit, alpha isoform	PPP2CA	5515	2
214168_s_at	tight junction protein 1 (zona occludens 1)	TJP1	7082	2
213213_at	death associated transcription factor 1	DATF1	11083	2
227203_at	F-box and leucine-rich repeat protein 17	FBXL17	64839	2
210014_x_at	isocitrate dehydrogenase 3 (NAD+) beta	IDH3B	3420	2
203937_s_at	TATA box binding protein (TBP)-associated factor, RNA polymerase I, C, 110kDa	TAF1C	9013	2
223398_at	chromosome 9 open reading frame 89	C9orf89	84270	2
218199_s_at	nucleolar protein family 6 (RNA-associated)	NOL6	65083	2
202500_at	DnaJ (Hsp40) homolog, subfamily B, member 2	DNAJB2	3300	2
219838_at	tetratricopeptide repeat domain 23	TTC23	64927	2
223092_at	ankylosis, progressive homolog (mouse)	ANKH	56172	2
209895_at	protein tyrosine phosphatase, non-receptor type 11 (Noonan syndrome 1)	PTPN11	5781	2
201247_at	sterol regulatory element binding transcription factor 2	SREBF2	6721	2
225277_at	solute carrier family 39 (zinc transporter), member 13	SLC39A13	91252	2
223622_s_at	hydroxypyruvate isomerase homolog (E. coli)	HYI	81888	2
226925_at	acid phosphatase-like 2	ACPL2	92370	2
201251_at	pyruvate kinase, muscle	PKM2	5315	2
218276_s_at	salvador homolog 1 (Drosophila)	SAV1	60485	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
59999_at	hypoxia-inducible factor 1, alpha subunit inhibitor	HIF1AN	55662	2
219338_s_at	leucine rich repeat containing 49	LRRC49	54839	2
219427_at	FAT tumor suppressor homolog 4 (Drosophila)	FAT4	79633	2
203614_at	UTP14, U3 small nucleolar ribonucleoprotein, homolog C (yeast)	UTP14C	9724	2
203565_s_at	menage a trois 1 (CAK assembly factor)	MNAT1	4331	2
209428_s_at	zinc finger protein-like 1	ZFPL1	7542	2
224699_s_at	family with sequence similarity 62 (C2 domain containing) member B	FAM62B	57488	2
217980_s_at	mitochondrial ribosomal protein L16	MRPL16	54948	2
226350_at	choroideremia-like (Rab escort protein 2)	CHML	1122	2
226209_at	NADH dehydrogenase (ubiquinone) flavoprotein 3, 10kDa	NDUFV3	4731	2
217957_at	gene trap locus 3 (mouse)	GTL3	29105	2
215199_at	caldesmon 1	CALD1	800	2
218908_at	alveolar soft part sarcoma chromosome region, candidate 1	ASPSCR1	79058	2
203339_at	solute carrier family 25 (mitochondrial carrier, Aralar), member 12	SLC25A12	8604	2
214170_x_at	fumarate hydratase	FH	2271	2
225779_at	solute carrier family 27 (fatty acid transporter), member 4	SLC27A4	10999	2
214780_s_at	myosin IXB	MYO9B	4650	2
225588_s_at	hypothetical protein BC009331	LOC92305	92305	2
202098_s_at	HMT1 hnRNP methyltransferase-like 1 (S. cerevisiae)	HRMT1L1	3275	2
207440_at	solute carrier family 35 (UDP-galactose transporter), member A2	SLC35A2	7355	2
203078_at	cullin 2	CUL2	8453	2
215046_at	hypothetical protein FLJ23861	FLJ23861	151050	2
203893_at	TAF9 RNA polymerase II, TATA box binding protein (TBP)-associated factor, 32kDa	TAF9	6880	2
225838_at	enhancer of polycomb homolog 2 (Drosophila)	EPC2	26122	2
226137_at	AT-binding transcription factor 1	ATBF1	463	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
218061_at	male-enhanced antigen 1	MEA1	4201	2
226380_at	Protein tyrosine phosphatase, non-receptor type 21	PTPN21	11099	2
201504_s_at	translin	TSN	7247	2
208767_s_at	lysosomal associated protein transmembrane 4 beta	LAPTM4B	55353	2
203955_at	KIAA0649	KIAA0649	9858	2
46270_at	ubiquitin associated protein 1	UBAP1	51271	2
219072_at	B-cell CLL/lymphoma 7C	BCL7C	9274	2
221647_s_at	resistance to inhibitors of cholinesterase 8 homolog A (C. elegans)	RIC8A	60626	2
230326_s_at	hypothetical protein HSPC138	HSPC138	51501	2
205878_at	POU domain, class 6, transcription factor 1	POU6F1	5463	2
40148_at	amyloid beta (A4) precursor protein-binding, family B, member 2 (Fe65-like)	APBB2	323	2
205141_at	angiogenin, ribonuclease, RNase A family, 5 ; ribonuclease, RNase A family, 4	ANG ; RNASE4	283 ; 6038	2
218607_s_at	SDA1 domain containing 1	SDAD1	55153	2
242789_at	phosphodiesterase 1A, calmodulin-dependent	PDE1A	5136	2
225791_at	selenocysteine lyase ; NEDD8-conjugating enzyme	SCLY ; NCE2	140739 ; 51540	2
225271_at	transmembrane protein 63B	TMEM63B	55362	2
202622_s_at	ataxin 2	ATXN2	6311	2
213133_s_at	glycine cleavage system protein H (aminomethyl carrier)	GCSH	2653	2
1554679_a_at	lysosomal associated protein transmembrane 4 beta	LAPTM4B	55353	2
213394_at	mitogen activated protein kinase binding protein 1	MAPKBP1	23005	2
218148_at	hypothetical protein FLJ13111	FLJ13111	80152	2
235635_at	Rho GTPase activating protein 5	ARHGAP5	394	2
203198_at	cyclin-dependent kinase 9 (CDC2-related kinase)	CDK9	1025	2
226666_at	Dishevelled associated activator of morphogenesis 1	DAAM1	23002	2
202397_at	nuclear transport factor 2	NUTF2	10204	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
200778_s_at	septin 2	Sep-02	4735	2
226987_at	RNA binding motif protein 15B	RBM15B	29890	2
216484_x_at	Hepatoma-derived growth factor (high-mobility group protein 1-like)	HDGF	3068	2
1554691_a_at	protein kinase C and casein kinase substrate in neurons 2	PACSIN2	11252	2
208680_at	peroxiredoxin 1	PRDX1	5052	2
210638_s_at	F-box protein 9	FBXO9	26268	2
211256_x_at	butyrophilin, subfamily 2, member A1	BTN2A1	11120	2
212128_s_at	dystroglycan 1 (dystrophin-associated glycoprotein 1)	DAG1	1605	2
203017_s_at	synovial sarcoma, X breakpoint 2 interacting protein	SSX2IP	117178	2
1566603_s_at	RNA pseudouridylate synthase domain containing 3	RPUSD3	285367	2
202947_s_at	glycophorin C (Gerbich blood group)	GYPC	2995	2
200913_at	protein phosphatase 1G (formerly 2C), magnesium-dependent, gamma isoform	PPM1G	5496	2
225196_s_at	mitochondrial ribosomal protein S26	MRPS26	64949	2
220182_at	solute carrier family 25 (mitochondrial carrier; phosphate carrier), member 23	SLC25A23	79085	2
221779_at	MICAL-like 1	MICAL-L1	85377	2
232649_at	Gliomedin	COLM	342035	2
223236_at	hypothetical protein DKFZp434K1421	DKFZP434K1421	84081	2
229312_s_at	G kinase anchoring protein 1	GKAP1	80318	2
35617_at	mitogen-activated protein kinase 7	MAPK7	5598	2
212719_at	PH domain and leucine rich repeat protein phosphatase	PHLPP	23239	2
1554016_a_at	hypothetical protein FLJ13154	FLJ13154	79650	2
210306_at	l(3)mbt-like (Drosophila)	L3MBTL	26013	2
201509_at	isocitrate dehydrogenase 3 (NAD+) beta	IDH3B	3420	2
212026_s_at	exocyst complex component 7	EXOC7	23265	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
213449_at	processing of precursor 1, ribonuclease P/MRP subunit (S. cerevisiae)	POP1	10940	2
223701_s_at	ubiquitin specific peptidase 47	USP47	55031	2
226696_at	retinoblastoma binding protein 9	RBBP9	10741	2
226151_x_at	crystallin, zeta (quinone reductase)-like 1	CRYZL1	9946	2
223057_s_at	exportin 5	XPO5	57510	2
206113_s_at	RAB5A, member RAS oncogene family	RAB5A	5868	2
214369_s_at	RAS guanyl releasing protein 2 (calcium and DAG-regulated)	RASGRP2	10235	2
1555122_at	G protein-coupled receptor 125	GPR125	166647	2
225679_at	chromosome 14 open reading frame 35	C14orf35	122830	2
218405_at	activator of basal transcription 1	ABT1	29777	2
218375_at	nudix (nucleoside diphosphate linked moiety X)-type motif 9	NUDT9	53343	2
222801_s_at	stromal antigen 3-like	FLJ13195	64940	2
202915_s_at	family with sequence similarity 20, member B	FAM20B	9917	2
222903_s_at	cytoplasmic polyadenylation element binding protein 1	CPEB1	64506	2
202862_at	fumarylacetoacetate hydrolase (fumarylacetoacetase)	FAH	2184	2
201081_s_at	phosphatidylinositol-4-phosphate 5-kinase, type II, beta	PIP5K2B	8396	2
200001_at	calpain, small subunit 1 ; calpain, small subunit 1	CAPNS1	826	2
201632_at	eukaryotic translation initiation factor 2B, subunit 1 alpha, 26kDa	EIF2B1	1967	2
208821_at	small nuclear ribonucleoprotein polypeptides B and B1	SNRPB	6628	2
219113_x_at	dehydrogenase/reductase (SDR family) member 10	DHRS10	51171	2
211051_s_at	exostoses (multiple)-like 3 ; exostoses (multiple)-like 3	EXTL3	2137	2
225289_at	signal transducer and activator of transcription 3 (acute-phase response factor)	STAT3	6774	2
225031_at	chromodomain helicase DNA binding protein 6	CHD6	84181	2
211467_s_at	nuclear factor I/B	NFIB	4781	2
200662_s_at	translocase of outer mitochondrial membrane 20 homolog (yeast)	TOMM20	9804	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
226764_at	hypothetical protein LOC152485	LOC152485	152485	2
201255_x_at	HLA-B associated transcript 3	BAT3	7917	2
226202_at	zinc finger protein 398	ZNF398	57541	2
44696_at	TBC1 domain family, member 13	TBC1D13	54662	2
214687_x_at	aldolase A, fructose-bisphosphate	ALDOA	226	2
216199_s_at	mitogen-activated protein kinase kinase kinase 4	MAP3K4	4216	2
216389_s_at	WD repeat domain 23	WDR23	80344	2
226386_at	chromosome 7 open reading frame 30	C7orf30	115416	2
209466_x_at	pleiotrophin (heparin binding growth factor 8, neurite growth-promoting factor 1)	PTN	5764	2
201162_at	insulin-like growth factor binding protein 7	IGFBP7	3490	2
204610_s_at	hepatitis delta antigen-interacting protein A	DIPA	11007	2
202088_at	solute carrier family 39 (zinc transporter), member 6	SLC39A6	25800	2
232662_x_at	Chromosome 10 open reading frame 58	C10orf58	84293	2
218229_s_at	pogo transposable element with KRAB domain	POGK	57645	2
231857_s_at	hypothetical protein FLJ21839	FLJ21839	60509	2
202405_at	TIA1 cytotoxic granule-associated RNA binding protein-like 1	TIAL1	7073	2
232207_at	hypothetical protein LOC285749	LOC285749	285749	2
1555216_a_at	LOC440450	LOC440450	440450	2
1553679_s_at	vitamin K epoxide reductase complex, subunit 1-like 1	VKORC1L1	154807	2
212590_at	related RAS viral (r-ras) oncogene homolog 2	RRAS2	22800	2
201388_at	proteasome (prosome, macropain) 26S subunit, non-ATPase, 3	PSMD3	5709	2
203151_at	microtubule-associated protein 1A	MAP1A	4130	2
212329_at	SREBP cleavage-activating protein	SCAP	22937	2
219919_s_at	slingshot homolog 3 (Drosophila)	SSH3	54961	2
212069_s_at	KIAA0515	KIAA0515	84726	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
228614_at	hypothetical protein LOC205251	LOC205251	205251	2
214383_x_at	kelch domain containing 3	KLHDC3	116138	2
226082_s_at	splicing factor, arginine/serine-rich 15	SFRS15	57466	2
238818_at	KIAA1429	KIAA1429	25962	2
219120_at	hypothetical protein FLJ21945	FLJ21945	80304	2
218497_s_at	ribonuclease H1	RNASEH1	246243	2
1558109_x_at	chromosome 20 open reading frame 80	C20orf80	91222	2
208353_x_at	ankyrin 1, erythrocytic	ANK1	286	2
209055_s_at	CDC5 cell division cycle 5-like (S. pombe)	CDC5L	988	2
228301_x_at	NADH dehydrogenase (ubiquinone) 1 beta subcomplex, 10, 22kDa	NDUFB10	4716	2
200993_at	importin 7	IPO7	10527	2
229068_at	chaperonin containing TCP1, subunit 5 (epsilon)	CCT5	22948	2
203959_s_at	zinc finger and BTB domain containing 40	ZBTB40	9923	2
218341_at	phosphopantothenoylcysteine synthetase	PPCS	79717	2
225457_s_at	DKFZP564I1171 protein	DKFZP564I1171	25845	2
203933_at	RAB11 family interacting protein 3 (class II)	RAB11FIP3	9727	2
207629_s_at	rho/rac guanine nucleotide exchange factor (GEF) 2	ARHGEF2	9181	2
223811_s_at	chromosome 7 open reading frame 20	C7orf20	51608	2
210094_s_at	par-3 partitioning defective 3 homolog (C. elegans)	PARD3	56288	2
227963_at	FLJ35696 protein	FLJ35696	388341	2
221822_at	hypothetical protein BC011981	LOC112869	112869	2
204381_at	low density lipoprotein receptor-related protein 3	LRP3	4037	2
220974_x_at	sideroflexin 3 ; sideroflexin 3	SFXN3	81855	2
224940_s_at	pregnancy-associated plasma protein A, pappalysin 1	PAPPA	5069	2
208880_s_at	chromosome 20 open reading frame 14	C20orf14	24148	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
225048_at	PHD finger protein 10	PHF10	55274	2
209668_x_at	carboxylesterase 2 (intestine, liver)	CES2	8824	2
213043_s_at	thyroid hormone receptor associated protein 4	THRAP4	9862	2
229100_s_at	translocase of inner mitochondrial membrane 22 homolog (yeast)	TIMM22	29928	2
49077_at	protein phosphatase methylesterase-1	PME-1	51400	2
217802_s_at	nuclear casein kinase and cyclin-dependent kinase substrate 1	NUCKS1	64710	2
208620_at	poly(rC) binding protein 1	PCBP1	5093	2
219576_at	hypothetical protein FLJ12649	FLJ12649	79649	2
226297_at	Homeodomain interacting protein kinase 3	HIPK3	10114	2
217734_s_at	WD repeat domain 6	WDR6	11180	2
218339_at	mitochondrial ribosomal protein L22	MRPL22	29093	2
224707_at	putative nuclear protein ORF1-FL49	ORF1-FL49	84418	2
213104_at	hypothetical protein MGC24381	MGC24381	115939	2
216511_s_at	transcription factor 7-like 2 (T-cell specific, HMG-box)	TCF7L2	6934	2
203478_at	NADH dehydrogenase (ubiquinone) 1, subcomplex unknown, 1, 6kDa	NDUFC1	4717	2
225267_at	karyopherin alpha 4 (importin alpha 3)	KPNA4	3840	2
223249_at	claudin 12	CLDN12	9069	2
203054_s_at	T-cell leukemia translocation altered gene	TCTA	6988	2
224690_at	chromosome 20 open reading frame 108	C20orf108	116151	2
212441_at	KIAA0232 gene product	KIAA0232	9778	2
208002_s_at	acyl-CoA thioesterase 7	ACOT7	11332	2
226295_at	uncharacterized hematopoietic stem/progenitor cells protein MDS028	MDS028	55846	2
201080_at	Phosphatidylinositol-4-phosphate 5-kinase, type II, beta	PIP5K2B	8396	2
214263_x_at	polymerase (RNA) II (DNA directed) polypeptide C, 33kDa	POLR2C	5432	2
227573_s_at	obscurin-like 1	OBSL1	23363	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
200684_s_at	ubiquitin-conjugating enzyme E2L 3	UBE2L3	7332	2
223315_at	netrin 4	NTN4	59277	2
203278_s_at	PHD finger protein 21A	PHF21A	51317	2
242207_at	Chromosome 9 open reading frame 12	C9orf12	64768	2
224763_at	ribosomal protein L37	RPL37	6167	2
201076_at	NHP2 non-histone chromosome protein 2-like 1 (S. cerevisiae)	NHP2L1	4809	2
202810_at	developmentally regulated GTP binding protein 1	DRG1	4733	2
216833_x_at	glycophorin B (includes Ss blood group) ; glycophorin E	GYPB ; GYPE	2994 ; 2996	2
213943_at	twist homolog 1 (acrocephalosyndactyly 3; Saethre-Chotzen syndrome) (Drosophila)	TWIST1	7291	2
202536_at	chromatin modifying protein 2B	CHMP2B	25978	2
205133_s_at	heat shock 10kDa protein 1 (chaperonin 10)	HSPE1	3336	2
211684_s_at	dynein, cytoplasmic, intermediate polypeptide 2	DNCI2	1781	2
203512_at	trafficking protein particle complex 3	TRAPPC3	27095	2
201135_at	enoyl Coenzyme A hydratase, short chain, 1, mitochondrial	ECHS1	1892	2
235263_at	DKFZp434A0131 protein	DKFZP434A0131	54441	2
217564_s_at	carbamoyl-phosphate synthetase 1, mitochondrial	CPS1	1373	2
212092_at	paternally expressed 10	PEG10	23089	2
230660_at	SERTA domain containing 4	SERTAD4	56256	2
228002_at	isopentenyl-diphosphate delta isomerase 2	IDI2	91734	2
219353_at	NHL repeat containing 2	NHLRC2	374354	2
209362_at	SRB7 suppressor of RNA polymerase B homolog (yeast)	SURB7	9412	2
211950_at	retinoblastoma-associated factor 600	RBAF600	23352	2
215464_s_at	Tax1 (human T-cell leukemia virus type I) binding protein 3	TAX1BP3	30851	2
203016_s_at	synovial sarcoma, X breakpoint 2 interacting protein	SSX2IP	117178	2
226254_s_at	KIAA1430	KIAA1430	57587	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
40560_at	T-box 2	TBX2	6909	2
228949_at	chromosome 1 open reading frame 139	C1orf139	79971	2
211955_at	RAN binding protein 5	RANBP5	3843	2
201817_at	ubiquitin protein ligase E3C	UBE3C	9690	2
218955_at	BRF2, subunit of RNA polymerase III transcription initiation factor, BRF1-like	BRF2	55290	2
220145_at	ASAP	FLJ21159	79884	2
225317_at	Importin 7	IPO7	10527	2
231130_at	acyl-Coenzyme A binding domain containing 6	ACBD6	84320	2
200992_at	FK506 binding protein 7	FKBP7	51661	2
218752_at	importin 7	IPO7	10527	2
51192_at	zinc finger, matrin type 5	ZMAT5	55954	2
211475_s_at	slingshot homolog 3 (Drosophila)	SSH3	54961	2
1553140_at	BCL2-associated athanogene	BAG1	573	2
225889_at	pelota homolog (Drosophila)	PELO	53918	2
219636_s_at	AE binding protein 2	AEBP2	121536	2
213058_at	armadillo repeat containing 9	ARMC9	80210	2
225772_s_at	KIAA1043 protein	KIAA1043	23331	2
208742_s_at	hypothetical protein MGC14288	MGC14288	84987	2
225135_at	sin3-associated polypeptide, 18kDa	SAP18	10284	2
225421_at	SIN3 homolog A, transcription regulator (yeast)	SIN3A	25942	2
228261_at	aminoacylase 1-like 2	ACY1L2	135293	2
224749_at	mindbomb homolog 2 (Drosophila)	MIB2	142678	2
212559_at	chromosome 16 open reading frame 9	C16orf9	83986	2
201220_x_at	protein kinase, cAMP-dependent, regulatory, type I, beta	PRKAR1B	5575	2
217814_at	C-terminal binding protein 2	CTBP2	1488	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
222409_at	GK001 protein	GK001	57003	2
234921_at	coronin, actin binding protein, 1C	CORO1C	23603	2
212369_at	FLJ26175 protein	FLJ26175	388566	2
59697_at	zinc finger protein 384	ZNF384	171017	2
202646_s_at	RAB15, member RAS onocogene family	RAB15	376267	2
214179_s_at	cold shock domain containing E1, RNA-binding	CSDE1	7812	2
235634_at	nuclear factor (erythroid-derived 2)-like 1	NFE2L1	4779	2
212309_at	purine-rich element binding protein G	PURG	29942	2
225038_s_at	cytoplasmic linker associated protein 2	CLASP2	23122	2
201754_at	surfeit 6	SURF6	6838	2
225863_s_at	cytochrome c oxidase subunit VIc	COX6C	1345	2
227998_at	chromosome 19 open reading frame 12	C19orf12	83636	2
203602_s_at	S100 calcium binding protein A16	S100A16	140576	2
221812_at	zinc finger and BTB domain containing 17	ZBTB17	7709	2
225268_at	F-box protein 42	FBXO42	54455	2
200676_s_at	karyopherin alpha 4 (importin alpha 3)	KPNA4	3840	2
210574_s_at	ubiquitin-conjugating enzyme E2L 3	UBE2L3	7332	2
224560_at	nuclear distribution gene C homolog (A. nidulans)	NUDC	10726	2
213132_s_at	TIMP metallopeptidase inhibitor 2	TIMP2	7077	2
218225_at	malonyl-CoA:acyl carrier protein transacylase, mitochondrial	MT	27349	2
203038_at	signaling intermediate in Toll pathway, evolutionarily conserved	SITPEC	51295	2
214876_s_at	protein tyrosine phosphatase, receptor type, K	PTPRK	5796	2
209465_x_at	tubulin, gamma complex associated protein 5	TUBGCP5	114791	2
227449_at	pleiotrophin (heparin binding growth factor 8, neurite growth-promoting factor 1)	PTN	5764	2
228397_at	EPH receptor A4	EPHA4	2043	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
225735_at	taurine upregulated gene 1	TUG1	55000	2
201030_x_at	KIAA1223 protein	KIAA1223	57182	2
222704_at	lactate dehydrogenase B	LDHB	3945	2
235068_at	polymerase (RNA) I polypeptide A, 194kDa	POLR1A	25885	2
202559_x_at	zinc finger, DHHC-type containing 21	ZDHHC21	340481	2
213946_s_at	chromosome 1 open reading frame 77	C1orf77	26097	2
225866_at	obscurin-like 1	OBSL1	23363	2
212218_s_at	brix domain containing 1	BXDC1	84154	2
1554106_at	fatty acid synthase	FASN	2194	2
219825_at	amyotrophic lateral sclerosis 2 (juvenile) chromosome region, candidate 16	ALS2CR16	130029	2
208316_s_at	cytochrome P450, family 26, subfamily B, polypeptide 1	CYP26B1	56603	2
218074_at	oculocerebrorenal syndrome of Lowe	OCRL	4952	2
227470_at	family with sequence similarity 96, member B	FAM96B	51647	2
209186_at	zinc finger protein 553	ZNF553	197407	2
213361_at	ATPase, Ca++ transporting, cardiac muscle, slow twitch 2	ATP2A2	488	2
200910_at	tudor domain containing 7	TDRD7	23424	2
50376_at	chaperonin containing TCP1, subunit 3 (gamma)	CCT3	7203	2
228084_at	zinc finger protein 444	ZNF444	55311	2
228813_at	histone deacetylase 4	HDAC4	9759	2
208696_at	chaperonin containing TCP1, subunit 5 (epsilon)	CCT5	22948	2
1553995_a_at	5'-nucleotidase, ecto (CD73)	NT5E	4907	2
212300_at	taxilin alpha	TXLNA	200081	2
228992_at	Mediator of RNA polymerase II transcription, subunit 28 homolog (yeast)	MED28	80306	2
228423_at	ASAP	FLJ21159	79884	2
207732_s_at	discs, large homolog 3 (neuroendocrine-dlg, Drosophila)	DLG3	1741	2
217608_at	p18 splicing regulatory protein	P18SRP	285672	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
225184_at	AT rich interactive domain 1B (SWI1-like)	ARID1B	57492	2
226319_s_at	THO complex 4	THOC4	10189	2
219399_at	lin-7 homolog C (C. elegans)	LIN7C	55327	2
215096_s_at	esterase D/formylglutathione hydrolase	ESD	2098	2
212324_s_at	vacuolar protein sorting 13D (yeast)	VPS13D	55187	2
1555702_a_at	ST3 beta-galactoside alpha-2,3-sialyltransferase 3	ST3GAL3	6487	2
200786_at	proteasome (prosome, macropain) subunit, beta type, 7	PSMB7	5695	2
1555831_s_at	leucine rich repeat containing 41	LRRC41	10489	2
229009_at	sine oculis homeobox homolog 5 (Drosophila)	SIX5	147912	2
215427_s_at	zinc finger, CCHC domain containing 14	ZCCHC14	23174	2
207268_x_at	abl interactor 2	ABI2	10152	2
229038_at	CWF19-like 1, cell cycle control (S. pombe)	CWF19L1	55280	2
211871_x_at	guanine nucleotide binding protein (G protein), beta 5	GNB5	10681	2
218089_at	chromosome 20 open reading frame 4	C20orf4	25980	2
208619_at	damage-specific DNA binding protein 1, 127kDa	DDB1	1642	2
204303_s_at	KIAA0427	KIAA0427	9811	2
203718_at	neuropathy target esterase	NTE	10908	2
238515_at	Nudix (nucleoside diphosphate linked moiety X)-type motif 16	FLJ31265	131870	2
208765_s_at	heterogeneous nuclear ribonucleoprotein R	HNRPR	10236	2
205606_at	low density lipoprotein receptor-related protein 6	LRP6	4040	2
217225_x_at	NODAL modulator 2	NOMO2	283820	2
206355_at	guanine nucleotide binding protein (G protein), alpha activating activity polypeptide, olfactory type	GNAL	2774	2
205412_at	acetyl-Coenzyme A acetyltransferase 1 (acetoacetyl Coenzyme A thiolase)	ACAT1	38	2
219157_at	kelch-like 2, Mayven (Drosophila)	KLHL2	11275	2
238653_at	Leucine-rich repeats and immunoglobulin-like domains 2	LRIG2	9860	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
208830_s_at	suppressor of Ty 6 homolog (S. cerevisiae)	SUPT6H	6830	2
221759_at	glucose 6 phosphatase, catalytic, 3	G6PC3	92579	2
201186_at	low density lipoprotein receptor-related protein associated protein 1	LRPAP1	4043	2
200894_s_at	FK506 binding protein 4, 59kDa	FKBP4	2288	2
212234_at	additional sex combs like 1 (Drosophila)	ASXL1	171023	2
218442_at	tetratricopeptide repeat domain 4	TTC4	7268	2
225560_at	protein-O-mannosyltransferase 2	POMT2	29954	2
202932_at	v-yes-1 Yamaguchi sarcoma viral oncogene homolog 1	YES1	7525	2
213313_at	RAB GTPase activating protein 1	RABGAP1	23637	2
226183_at	Glycogen synthase kinase 3 beta	GSK3B	2932	2
202675_at	succinate dehydrogenase complex, subunit B, iron sulfur (Ip)	SDHB	6390	2
1554291_at	KIAA0701 protein	KIAA0701	23074	2
209715_at	chromobox homolog 5 (HP1 alpha homolog, Drosophila)	CBX5	23468	2
203051_at	bromo adjacent homology domain containing 1	BAHD1	22893	2
223370_at	pleckstrin homology domain containing, family A	PLEKHA3	65977	2
228662_at	Suppressor of cytokine signaling 7	SOCS7	30837	2
218997_at	polymerase (RNA) I associated factor 1	PRAF1	64425	2
219261_at	chromosome 7 open reading frame 26	C7orf26	79034	2
AFFX-HUMGAPDH	glyceraldehyde-3-phosphate dehydrogenase	GAPDH	2597	2
222800_at	tRNA selenocysteine associated protein	SECP43	54952	2
231974_at	myeloid/lymphoid or mixed-lineage leukemia 2	MLL2	8085	2
209296_at	protein phosphatase 1B (formerly 2C), magnesium-dependent, beta isoform	PPM1B	5495	2
220517_at	vacuolar protein sorting 13C (yeast)	VPS13C	54832	2
215749_s_at	golgi reassembly stacking protein 1, 65kDa	GORASP1	64689	2
210986_s_at	tropomyosin 1 (alpha)	TPM1	7168	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
220500_s_at	RAB, member of RAS oncogene family-like 2B ; RAB, member of RAS oncogene family-like 2A	RABL2B ; RABL2A	11158 ; 11159	2
222019_at	HLA class II region expressed gene KE2	HKE2	10471	2
212954_at	dual-specificity tyrosine-(Y)-phosphorylation regulated kinase 4	DYRK4	8798	2
203611_at	telomeric repeat binding factor 2	TERF2	7014	2
213694_at	round spermatid basic protein 1	RSBN1	54665	2
202048_s_at	chromobox homolog 6	CBX6	23466	2
210266_s_at	tripartite motif-containing 33	TRIM33	51592	2
224727_at	hypothetical protein LOC284361	LOC284361	284361	2
209814_at	zinc finger protein 330	ZNF330	27309	2
200046_at	defender against cell death 1 ; defender against cell death 1	DAD1	1603	2
225658_at	hypothetical protein LOC339745	LOC339745	339745	2
217969_at	chromosome 11 open reading frame2	C11orf2	738	2
225170_at	WD repeat domain 5	WDR5	11091	2
201962_s_at	ring finger protein 41	RNF41	10193	2
227270_at	hypothetical protein LOC285550	LOC285550	285550	2
208950_s_at	aldehyde dehydrogenase 7 family, member A1	ALDH7A1	501	2
218697_at	NCK interacting protein with SH3 domain	NCKIPSD	51517	2
201581_at	thioredoxin domain containing 13	TXNDC13	56255	2
204149_s_at	glutathione S-transferase M4	GSTM4	2948	2
224370_s_at	calcyphosine 2 ; calcyphosine 2	CAPS2	84698	2
203875_at	SWI/SNF related, matrix associated, actin dependent regulator of chromatin	SMARCA1	6594	2
202136_at	zinc finger, MYND domain containing 11	ZMYND11	10771	2
226781_at	hypothetical protein HSPC268	HSPC268	154791	2
210142_x_at	flotillin 1	FLOT1	10211	2
238929_at	Splicing factor, arginine/serine-rich, 46kD	SRP46	10929	2
201696_at	splicing factor, arginine/serine-rich 4	SFRS4	6429	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
213286_at	zinc finger RNA binding protein	ZFR	51663	2
209982_s_at	neurexin 2	NRXN2	9379	2
202686_s_at	AXL receptor tyrosine kinase	AXL	558	2
220968_s_at	tetraspanin 9 ; tetraspanin 9	TSPAN9	10867	2
213838_at	nucleolar protein 7, 27kDa	NOL7	51406	2
221538_s_at	plexin A1	PLXNA1	5361	2
204690_at	syntaxin 8	STX8	9482	2
225370_at	pygopus homolog 2 (Drosophila)	PYGO2	90780	2
235196_at	Cell division cycle 73, Paf1/RNA polymerase II complex component, homolog (S. cerevisiae)	HRPT2	79577	2
224993_at	hypothetical protein from EUROIMAGE 1669387	LOC56930	56930	2
208774_at	casein kinase 1, delta	CSNK1D	1453	2
201797_s_at	valyl-tRNA synthetase	VARS	7407	2
212762_s_at	transcription factor 7-like 2 (T-cell specific, HMG-box)	TCF7L2	6934	2
221699_s_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 50 ; DEAD (Asp-Glu-Ala-Asp) box polypeptide 50	DDX50	79009	2
218898_at	family with sequence similarity 57, member A	FAM57A	79850	2
215198_s_at	caldesmon 1	CALD1	800	2
208923_at	cytoplasmic FMR1 interacting protein 1	CYFIP1	23191	2
AFFX-HSAC07	actin, beta	ACTB	60	2
202220_at	KIAA0907	KIAA0907	22889	2
221851_at	hypothetical protein BC002926	LOC90379	90379	2
202315_s_at	breakpoint cluster region	BCR	613	2
223150_s_at	protein tyrosine phosphatase, non-receptor type 23	PTPN23	25930	2
204640_s_at	speckle-type POZ protein	SPOP	8405	2
222439_s_at	thyroid hormone receptor associated protein 3	THRAP3	9967	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
218105_s_at	mitochondrial ribosomal protein L4	MRPL4	51073	2
217913_at	vacuolar protein sorting 4A (yeast)	VPS4A	27183	2
225103_at	mitochondrial ribosomal protein L38	MRPL38	64978	2
219348_at	uncharacterized hematopoietic stem/progenitor cells protein MDS032	MDS032	55850	2
202408_s_at	PRP31 pre-mRNA processing factor 31 homolog (yeast)	PRPF31	26121	2
200844_s_at	peroxiredoxin 6	PRDX6	9588	2
217185_s_at	zinc finger protein 259	ZNF259	8882	2
221564_at	HMT1 hnRNP methyltransferase-like 1 (S. cerevisiae)	HRMT1L1	3275	2
225611_at	microtubule associated serine/threonine kinase family member 4	MAST4	23227	2
201057_s_at	golgi autoantigen, golgin subfamily b, macrogolgin (with transmembrane signal), 1	GOLGB1	2804	2
212053_at	KIAA0251 protein	KIAA0251	23042	2
200966_x_at	aldolase A, fructose-bisphosphate	ALDOA	226	2
214738_s_at	NIMA (never in mitosis gene a)- related kinase 9	NEK9	91754	2
201472_at	von Hippel-Lindau binding protein 1	VBP1	7411	2
242363_at	Dynein, cytoplasmic, intermediate polypeptide 2	DNCI2	1781	2
209702_at	fatso	FTO	79068	2
227866_at	RNA binding motif protein 16	RBM16	22828	2
228480_at	VAMP (vesicle-associated membrane protein)-associated protein A, 33kDa	VAPA	9218	2
224163_s_at	DNA methyltransferase 1 associated protein 1	DMAP1	55929	2
204166_at	KIAA0963	KIAA0963	22904	2
212432_at	GrpE-like 1, mitochondrial (E. coli)	GRPEL1	80273	2
223469_at	hypothetical protein MGC10812	MGC10812	83542	2
208627_s_at	Y box binding protein 1	YBX1	4904	2
210208_x_at	HLA-B associated transcript 3	BAT3	7917	2
226862_at	methyl-CpG binding domain protein 1	MBD1	4152	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
241872_at	SH3-domain GRB2-like (endophilin) interacting protein 1	DKFZp761D221	84251	2
1555790_a_at	zinc finger protein like ; hypothetical protein FLJ38482	ZFPL ; FLJ38482	162967 ; 201931	2
202121_s_at	chromatin modifying protein 2A	CHMP2A	27243	2
203884_s_at	RAB11 family interacting protein 2 (class I)	RAB11FIP2	22841	2
212819_at	ankyrin repeat and SOCS box-containing 1	ASB1	51665	2
226857_at	Rho guanine nucleotide exchange factor (GEF) 19	ARHGEF19	128272	2
218946_at	HIRA interacting protein 5	HIRIP5	27247	2
226826_at	LSM11, U7 small nuclear RNA associated	LSM11	134353	2
212109_at	chromosome 16 open reading frame 34	C16orf34	90861	2
208867_s_at	casein kinase 1, alpha 1	CSNK1A1	1452	2
227500_at	F-box and leucine-rich repeat protein 18	FBXL18	80028	2
222863_at	zinc finger and BTB domain containing 10	ZBTB10	65986	2
202355_s_at	general transcription factor IIF, polypeptide 1, 74kDa	GTF2F1	2962	2
227669_at	Brain protein 44	DKFZP564B167	25874	2
226726_at	O-acyltransferase (membrane bound) domain containing 2	OACT2	129642	2
212408_at	torsin A interacting protein 1	TOR1AIP1	26092	2
226946_at	hypothetical protein FLJ30596	FLJ30596	133686	2
223027_at	sorting nexin 9	SNX9	51429	2
238906_s_at	ras homolog gene family, member J	RHOJ	57381	2
217804_s_at	interleukin enhancer binding factor 3, 90kDa	ILF3	3609	2
222391_at	transmembrane protein 30A	TMEM30A	55754	2
203262_s_at	family with sequence similarity 50, member A	FAM50A	9130	2
212402_at	KIAA0853	KIAA0853	23091	2
212987_at	F-box protein 9	FBXO9	26268	2
208719_s_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 17	DDX17	10521	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
228096_at	chromosome 1 open reading frame 151	C1orf151	440574	2
211783_s_at	metastasis associated 1 ; metastasis associated 1	MTA1	9112	2
236104_at	Heterogeneous nuclear ribonucleoprotein L-like	HNRPLL	92906	2
212037_at	pinin, desmosome associated protein	PNN	5411	2
1555015_a_at	zinc finger protein 398	ZNF398	57541	2
201471_s_at	sequestosome 1	SQSTM1	8878	2
200802_at	seryl-tRNA synthetase	SARS	6301	2
203785_s_at	DEAD (Asp-Glu-Ala-Asp) box polypeptide 28	DDX28	55794	2
235846_at	RAD54 homolog B (S. cerevisiae)	RAD54B	25788	2
1559946_s_at	RuvB-like 2 (E. coli)	RUVBL2	10856	2
208806_at	chromodomain helicase DNA binding protein 3	CHD3	1107	2
200072_s_at	heterogeneous nuclear ribonucleoprotein M ; heterogeneous nuclear ribonucleoprotein M	HNRPM	4670	2
201594_s_at	protein phosphatase 4, regulatory subunit 1	PPP4R1	9989	2
219366_at	apoptosis, caspase activation inhibitor	AVEN	57099	2
227113_at	alcohol dehydrogenase, iron containing, 1	ADHFE1	137872	2
202161_at	protein kinase N1	PKN1	5585	2
225232_at	myotubularin related protein 12	MTMR12	54545	2
206348_s_at	pyruvate dehydrogenase kinase, isoenzyme 3	PDK3	5165	2
204460_s_at	RAD1 homolog (S. pombe)	RAD1	5810	2
203832_at	small nuclear ribonucleoprotein polypeptide F	SNRPF	6636	2
205449_at	SAC3 domain containing 1	SAC3D1	29901	2
224684_at	Sorting nexin 12	SNX12	29934	2
225106_s_at	hypothetical protein FLJ10826	FLJ10826	55239	2
201947_s_at	chaperonin containing TCP1, subunit 2 (beta)	CCT2	10576	2
201155_s_at	mitofusin 2	MFN2	9927	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
225347_at	ADP-ribosylation factor-like 10B	ARL10B	127829	2
203476_at	trophoblast glycoprotein	TPBG	7162	2
204104_at	small nuclear RNA activating complex, polypeptide 2, 45kDa	SNAPC2	6618	2
226820_at	FLJ25476 protein	FLJ25476	149076	2
224907_s_at	SH3-domain GRB2-like endophilin B2	SH3GLB2	56904	2
222526_at	GATA zinc finger domain containing 2A	p66alpha	54815	2
204383_at	DiGeorge syndrome critical region gene 14	DGCR14	8220	2
226481_at	Vpr-binding protein	VprBP	9730	2
224755_at	SM-11044 binding protein	SMBP	56889	2
217832_at	synaptotagmin binding, cytoplasmic RNA interacting protein	SYNCRIP	10492	2
212752_at	cytoplasmic linker associated protein 1	CLASP1	23332	2
225076_s_at	KIAA1404 protein	KIAA1404	57169	2
224473_x_at	leucine zipper, putative tumor suppressor 2 ; leucine zipper, putative tumor suppressor 2	LZTS2	84445	2
214315_x_at	calreticulin	CALR	811	2
202669_s_at	ephrin-B2	EFNB2	1948	2
226976_at	Karyopherin alpha 6 (importin alpha 7)	KPNA6	23633	2
205300_s_at	U11/U12 snRNP 35K	U1SNRNPBP	11066	2
213259_s_at	sterile alpha and TIR motif containing 1	SARM1	23098	2
222425_s_at	polymerase (DNA-directed), delta interacting protein 2	POLDIP2	26073	2
220150_s_at	chromosome 6 open reading frame 60	C6orf60	79632	2
216060_s_at	dishevelled associated activator of morphogenesis 1	DAAM1	23002	2
226580_at	breast cancer metastasis-suppressor 1-like	BRMS1L	84312	2
212166_at	exportin 7	XPO7	23039	2
209113_s_at	high-mobility group 20B	HMG20B	10362	2
31846_at	ras homolog gene family, member D	RHOD	29984	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
201119_s_at	cytochrome c oxidase subunit 8A (ubiquitous)	COX8A	1351	2
220198_s_at	eukaryotic translation initiation factor 5A2	EIF5A2	56648	2
217816_s_at	PEST-containing nuclear protein	PCNP	57092	2
207320_x_at	staufen, RNA binding protein (Drosophila)	STAU	6780	2
214464_at	CDC42 binding protein kinase alpha (DMPK-like)	CDC42BPA	8476	2
218626_at	eukaryotic translation initiation factor 4E nuclear import factor 1	EIF4ENIF1	56478	2
218982_s_at	mitochondrial ribosomal protein S17	MRPS17	51373	2
232837_at	kinesin family member 13A	KIF13A	63971	2
200718_s_at	S-phase kinase-associated protein 1A (p19A)	SKP1A	6500	2
213405_at	RAB22A, member RAS oncogene family	RAB22A	57403	2
219467_at	hypothetical protein FLJ20125	FLJ20125	54826	2
1553216_at	zinc finger protein 41	ZNF41	7592	2
220734_s_at	hypothetical protein MGC10334	MGC10334	80772	2
200636_s_at	protein tyrosine phosphatase, receptor type, F	PTPRF	5792	2
210337_s_at	ATP citrate lyase	ACLY	47	2
201315_x_at	interferon induced transmembrane protein 2 (1-8D)	IFITM2	10581	2
217780_at	PTD008 protein	PTD008	51398	2
224706_at	KIAA2013	KIAA2013	90231	2
200749_at	RAN, member RAS oncogene family ; similar to Ras-related nuclear protein	RAN ; LOC391717	391717 ; 5901	2
208964_s_at	fatty acid desaturase 1	FADS1	3992	2
200787_s_at	phosphoprotein enriched in astrocytes 15	PEA15	8682	2
210474_s_at	cell division cycle 2-like 1 (PITSLRE proteins) ; cell division cycle 2-like 2 (PITSLRE proteins)	CDC2L1 ; CDC2L2	984 ; 985	2
213832_at	Clone 24405 mRNA sequence			2
233123_at	Solute carrier family 40 (iron-regulated transporter), member 1	SLC40A1	30061	2
202764_at	stromal interaction molecule 1	STIM1	6786	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
222735_at	transmembrane protein 38B	TMEM38B	55151	2
224659_at	selenoprotein N, 1	SEPN1	57190	2
203342_at	translocase of inner mitochondrial membrane 17 homolog B (yeast)	TIMM17B	10245	2
213224_s_at	hypothetical protein LOC92482	LOC92482	92482	2
222551_s_at	chromosome 8 open reading frame 33	C8orf33	65265	2
209486_at	disrupter of silencing 10	SAS10	57050	2
211855_s_at	solute carrier family 25 (mitochondrial carrier, brain), member 14	SLC25A14	9016	2
201391_at	TNF receptor-associated protein 1	TRAP1	10131	2
202472_at	mannose phosphate isomerase	MPI	4351	2
201842_s_at	EGF-containing fibulin-like extracellular matrix protein 1	EFEMP1	2202	2
212134_at	pleckstrin homology-like domain, family B, member 1	PHLDB1	23187	2
202012_s_at	exostoses (multiple) 2	EXT2	2132	2
223041_at	CD99 antigen-like 2	CD99L2	83692	2
226053_at	mitogen-activated protein kinase kinase 7	MAP2K7	5609	2
227378_x_at	hypothetical protein MGC13114	MGC13114	84326	2
225405_at	Heterogeneous nuclear ribonucleoprotein U-like 2	DKFZp762N1910	221092	2
1554868_s_at	PEST-containing nuclear protein	PCNP	57092	2
203519_s_at	UPF2 regulator of nonsense transcripts homolog (yeast)	UPF2	26019	2
204617_s_at	adrenocortical dysplasia homolog (mouse)	ACD	65057	2
218782_s_at	ATPase family, AAA domain containing 2	ATAD2	29028	2
209745_at	coenzyme Q7 homolog, ubiquinone (yeast)	COQ7	10229	2
223348_x_at	melanoma associated antigen (mutated) 1	MUM1	84939	2
218408_at	translocase of inner mitochondrial membrane 10 homolog (yeast)	TIMM10	26519	2
219186_at	zinc finger and BTB domain containing 7A	ZBTB7A	51341	2
202180_s_at	major vault protein	MVP	9961	2

Appendix E: Genes downregulated in AAA vs. NA (continued).

Probe	Gene description	Gene symbol	Entrez Gene ID	Fold change
224467_s_at	hypothetical protein MGC13096 ; hypothetical protein MGC13096	MGC13096	84306	2
231200_at	family with sequence similarity 61, member B	FAM61B	149986	2
201580_s_at	thioredoxin domain containing 13	TXNDC13	56255	2
216396_s_at	etoposide induced 2.4 mRNA	EI24	9538	2
203707_at	zinc finger protein 263	ZNF263	10127	2
205146_x_at	amyloid beta (A4) precursor protein-binding, family A, member 3 (X11-like 2)	APBA3	9546	2
203607_at	inositol polyphosphate-5-phosphatase F	INPP5F	22876	2
201945_at	furin (paired basic amino acid cleaving enzyme)	FURIN	5045	2
212161_at	adaptor-related protein complex 2, alpha 2 subunit	AP2A2	161	2
221847_at	LOC440123	LOC440123	440123	2
219518_s_at	elongation factor RNA polymerase II-like 3	ELL3	80237	2
202103_at	bromodomain containing 4	BRD4	23476	2
201774_s_at	chromosome condensation-related SMC-associated protein 1	CNAP1	9918	2
33494_at	electron-transferring-flavoprotein dehydrogenase	ETFDH	2110	2
235356_at	NHL repeat containing 2	NHLRC2	374354	2

Appendix F: Inflammatory genes in AAA vs. AOD

Upregulated Genes	Gene Symbol	Entrez Gene ID	Fold change
immunoglobulin heavy locus ; immunoglobulin heavy constant alpha 1	IGHA1	283650	18
Immunoglobulin lambda joining 3	IGLC2	3538	14
BCR downstream signaling 1	BRDG1	26228	10
Immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	IGJ	3512	8
membrane-spanning 4-domains, subfamily A, member 1	MS4A1	931	7
CD79A antigen (immunoglobulin-associated alpha)	CD79A	973	6
Paired box gene 5 (B-cell lineage specific activator)	PAX5	5079	5
membrane-spanning 4-domains, subfamily A, member 1	MS4A1	931	5
major histocompatibility complex, class II, DO beta	HLA-DOB	3112	5
complement component 3	C3	718	4
chemokine (C-X3-C motif) receptor 1	CX3CR1	1524	4
toll-like receptor 10	TLR10	81793	4
CD19	CD19	930	4
Ras homolog gene family, member H	RHOH	399	3
Spi-B transcription factor	SPIB	6689	3
X-box binding protein 1	XBP1	7494	3
ST6 beta-galactosamide alpha-2,6-sialyltranferase 1	ST6GAL1	6480	3
aldehyde oxidase 1	AOX1	316	3
absent in melanoma 2	AIM2	9447	3
Burkitt lymphoma receptor 1, GTP binding protein (chemokine (C-X-C motif) receptor 5)	BLR1	643	3
immunoglobulin heavy constant gamma 1 (G1m marker)	IGHG1	3500	3
C-type lectin domain family 2, member D	CLEC2D	29121	3
CD79B antigen (immunoglobulin-associated beta)	CD79B	974	3
Fas apoptotic inhibitory molecule 3	FAIM3	9214	2
ras homolog gene family, member H	RHOH	399	2
ryanodine receptor 1 (skeletal)	RYR1	6261	2
chemokine (C-C motif) ligand 13	CCL13	6357	2

Appendix F: Inflammatory genes in AAA vs. AOD (continued).

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
interleukin 2 receptor, gamma (severe combined immunodeficiency)	IL2RG	3561	2
ST6 beta-galactosamide alpha-2,6-sialyltranferase 1	ST6GAL1	6480	2
sema domain, immunoglobulin domain (Ig)	SEMA4D	10507	2
interleukin 7	IL7	3574	2

Downregulated Genes	Gene Symbol	Entrez Gene ID	Fold change
endothelial differentiation, sphingolipid G-protein-coupled receptor, 3	EDG3	1903	3
fibronectin 1	FN1	2335	3
tumor necrosis factor, alpha-induced protein 6	TNFAIP6	7130	3
carbohydrate (keratan sulfate Gal-6) sulfotransferase 1	CHST1	8534	3
peroxidasin homolog (Drosophila)	PXDN	7837	2
UL16 binding protein 2	ULBP2	80328	2
chemokine (C-C motif) receptor 1	CCR1	1230	2
solute carrier family 11 (proton-coupled divalent metal ion transporters), member 1	SLC11A1	6556	2
stabilin 1	STAB1	23166	2

Appendix G: Proteolytic genes in AAA vs. AOD

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2	B3GALT2	8707	9
activin A receptor, type IC	ACVR1C	130399	4
Matrix metallopeptidase 3	MMP-3	4314	3
ST6 beta-galactosamide alpha-2,6-sialyltranferase 1	ST6GAL1	6480	3
SEC11-like 3 (S. cerevisiae)	SEC11L3	90701	3
ryanodine receptor 1 (skeletal)	RYR1	6261	2
Cathepsin H	CTSH	1512	2
phenylalanine-tRNA synthetase-like, beta subunit	FARSLB	10056	2
ST6 beta-galactosamide alpha-2,6-sialyltranferase 1	ST6GAL1	6480	2
Ankyrin repeat and KH domain containing 1	ANKHD1	54882	2

Appendix G: Proteolytic genes in AAA vs. AOD (continued).

Downregulated Genes	Gene symbol	Entrez Gene ID	Fold change
folate hydrolase (prostate-specific membrane antigen) 1	FOLH1	2346	4
PDZ binding kinase	PBK	55872	3
Sulfatase 1	SULF1	23213	3
cathepsin L	CTSL	1514	3
phosphodiesterase 4D interacting protein (myomegalin)	PDE4DIP	9659	3
hepatocyte growth factor (hepapoietin A; scatter factor)	HGF	3082	3
TTK protein kinase	TTK	7272	3
apolipoprotein E	APOE	348	3
matrix metallopeptidase 14 (membrane-inserted)	MMP14	4323	2
ADAM metallopeptidase with thrombospondin type 1 motif, 9	ADAMTS9	56999	2
ADAM metallopeptidase domain 8 ; ADAM metallopeptidase domain 8	ADAM8	101	2
Protein phosphatase 3 (formerly 2B), catalytic subunit, alpha isoform (calcineurin A alpha)	PPP3CA	5530	2
aspartate beta-hydroxylase	ASPH	444	2
galactose-3-O-sulfotransferase 4	GAL3ST4	79690	2
bone morphogenetic protein 1	BMP1	649	2
ADAM metallopeptidase with thrombospondin type 1 motif, 6	ADAMTS6	11174	2
serpin peptidase inhibitor, clade H (heat shock protein 47), member 1, (collagen binding protein 1)	SERPINH1	871	2
procollagen-lysine 1, 2-oxoglutarate 5-dioxygenase 1	PLOD1	5351	2
lysyl-tRNA synthetase	KARS	3735	2
c-mer proto-oncogene tyrosine kinase	MERTK	10461	2
Insulin receptor	INSR	3643	2

Appendix H: Apoptotic genes in AAA vs. AOD

Upregulated Genes	Gene Symbol	Entrez Gene ID	Fold change
activin A receptor, type IC	ACVR1C	130399	4
mal, T-cell differentiation protein	MAL	4118	3
tumor protein p53 inducible nuclear protein 1	TP53INP1	94241	3
Fas apoptotic inhibitory molecule 3 ; Fas apoptotic inhibitory molecule 3	FAIM3	9214	2
ELL associated factor 2	EAF2	55840	2
ryanodine receptor 1 (skeletal)	RYR1	6261	2

Downregulated Genes	Gene Symbol	Entrez Gene ID	Fold change
angiopoietin-like 4	ANGPTL4	51129	7
Effector cell peptidase receptor 1	BIRC5	332	4
Sulfatase 1	SULF1	23213	3
LIM and senescent cell antigen-like domains 1	LIMS1	3987	3
apolipoprotein E	APOE	348	3
pleckstrin homology-like domain, family A, member 2	PHLDA2	7262	2

Appendix I: Angiogenic genes in AAA vs. AOD

Upregulated Genes	Gene Symbol	Entrez Gene ID	Fold change
homeo box D10	HOXD10	3236	4
homeo box A5	HOXA5	3202	2
DnaJ (Hsp40) homolog, subfamily B, member 9	DNAJB1	4189	2

Downregulated Genes	Gene Symbol	Entrez Gene ID	Fold change
angiopoietin-like 4	ANGPTL4	51129	7
plexin domain containing 1	PLXDC1	57125	2
angiopoietin 2	ANGPT2	285	2
stabilin 1	STAB1	23166	2
Fms-related tyrosine kinase 1 (vascular endothelial growth factor)	FLT1	2321	2

Appendix J: Inflammatory genes in AAA vs. NA

Upregulated Genes	Gene Symbol	Entrez Gene ID	Fold change
Immunoglobulin lambda joining 3	IGLC2	3538	79
Immunoglobulin kappa variable 1-5 ; Immunoglobulin kappa variable 1-5	IGKC	3514	55
immunoglobulin heavy constant mu	IGHM	3507	50
immunoglobulin kappa constant ; immunoglobulin kappa constant	IGKC	3514	47
immunoglobulin heavy locus ; immunoglobulin heavy constant gamma 1 (G1m marker)	IGHG1	3492	38
CD79A antigen (immunoglobulin-associated alpha)	CD79A	973	36
immunoglobulin heavy locus ; immunoglobulin heavy constant alpha 1	IGHA1	283650	26
Immunoglobulin J polypeptide, linker protein for immunoglobulin alpha and mu polypeptides	IGJ	3512	20
SLAM family member 7	SLAMF7	57823	19
BCR downstream signaling 1	BRDG1	26228	17
CD19 antigen	CD19	930	15
immunoglobulin lambda locus ; immunoglobulin lambda constant 1 (Mcg marker)	IGLC1	28793	14
Fas apoptotic inhibitory molecule 3 ; Fas apoptotic inhibitory molecule 3	FAIM3	9214	13
CD69 antigen (p60, early T-cell activation antigen)	CD69	969	12
tumor necrosis factor receptor superfamily, member 7 ;	TNFRSF7	939	11
Paired box gene 5 (B-cell lineage specific activator)	PAX5	5079	11
cytotoxic T-lymphocyte-associated protein 4	CTLA4	1493	10
regulator of G-protein signalling 1	RGS1	5996	9
CD3G antigen, gamma polypeptide (TiT3 complex)	CD3G	917	9
lymphocyte transmembrane adaptor 1	LAX1	54900	9
major histocompatibility complex, class II, DO beta	HLA-DOB	3112	9
chemokine (C-C motif) receptor 7 ; chemokine (C-C motif) receptor 7	CCR7	1236	8
ras homolog gene family, member H	RHOH	399	8
toll-like receptor 10	TLR10	81793	8

Appendix J: Inflammatory genes in AAA vs. NA (continued)

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
Interleukin 7 receptor	IL7R	3575	8
lymphocyte antigen 9	LY9	4063	7
chemokine (C-C motif) ligand 3	CCL3	414062	7
chemokine (C-C motif) ligand 5	CCL5	6352	7
regulator of G-protein signalling 1	RGS1	5996	7
cathepsin S	CTSS	1520	7
T cell receptor alpha locus	TRAC	28755	6
signaling threshold regulating transmembrane adaptor 1	SIT1	27240	6
interferon, gamma	IFNG	3458	6
absent in melanoma 2	AIM2	9447	6
T cell receptor beta variable 21-1	TRBV21-1	28566	6
Epstein-Barr virus induced gene 2 (lymphocyte-specific G protein-coupled receptor)	EBI2	1880	6
SP140 nuclear body protein	SP140	11262	6
T cell receptor beta variable 19 ; T cell receptor beta constant 1	TRBV19	28568	5
CD8 antigen, beta polypeptide 1 (p37)	CD8B1	926	5
chemokine (C-C motif) ligand 4	CCL4	6351	5
cytotoxic T-lymphocyte-associated protein 4	CTLA4	1493	5
zeta-chain (TCR) associated protein kinase 70kDa	ZAP70	7535	5
Spi-B transcription factor (Spi-1/PU.1 related)	SPIB	6689	5
CD2 antigen (p50), sheep red blood cell receptor ; CD2 antigen (p50), sheep red blood cell receptor	CD2	914	5
Fc fragment of IgG, low affinity IIIb, receptor (CD16b)	FCGR3B	2215	5
CD53 antigen	CD53	963	5
interleukin 2 receptor, gamma (severe combined immunodeficiency)	IL2RG	3561	5
lymphocyte-specific protein tyrosine kinase	LCK	3932	5
CD6 antigen ; CD6 antigen	CD6	923	5

Appendix J: Inflammatory genes in AAA vs. NA (continued)

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
lymphocyte antigen 6 complex, locus H	LY6H	4062	5
CD3D antigen, delta polypeptide (TiT3 complex)	CD3D	915	5
neutrophil cytosolic factor 1 (47kDa, chronic granulomatous disease, autosomal 1)	NCF1	4687	4
IL2-inducible T-cell kinase	ITK	3702	4
killer cell lectin-like receptor subfamily B, member 1 ;	KLRB1	3820	4
SH2 domain protein 1A, Duncan's disease (lymphoproliferative syndrome)	SH2D1A	4068	4
POU domain, class 2, transcription factor 2	POU2F2	5452	4
integrin, alpha L (antigen CD11A (p180)	ITGAL	3683	4
dipeptidylpeptidase 4 (CD26, adenosine deaminase complexing protein 2)	DPP4	1803	4
Beta-2-microglobulin	B2M	567	4
type 1 tumor necrosis factor receptor shedding aminopeptidase regulator	ARTS-1	51752	4
lymphotoxin beta (TNF superfamily, member 3)	LTB	4050	4
B-cell linker	BLNK	29760	4
apolipoprotein B mRNA editing enzyme, catalytic polypeptide-like 3G	APOBEC3G	60489	4
interleukin 16 (lymphocyte chemoattractant factor)	IL16	3603	4
major histocompatibility complex, class II, DM beta ;	HLA-DMB	3109	4
FYN binding protein (FYB-120/130)	FYB	2533	4
CD48 antigen (B-cell membrane protein) ; CD48 antigen (B-cell membrane protein)	CD48	962	4
adenosine A3 receptor	ADORA3	140	4
major histocompatibility complex, class II, DQ alpha 1	HLA-DQA1	3117	4
coagulation factor III (thromboplastin, tissue factor)	F3	2152	4
Guanylate binding protein 5	GBP5	115362	4
major histocompatibility complex, class II, DQ beta 1	HLA-DQB1	3119	4
X-box binding protein 1	XBP1	7494	3
Fc fragment of IgE, high affinity I, receptor for; alpha polypeptide	FCER1A	2205	3

Appendix J: Inflammatory genes in AAA vs. NA (continued)

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
lymphocyte-specific protein tyrosine kinase	LCK	3932	3
lymphocyte cytosolic protein 2 (SH2 domain containing leukocyte protein of 76kDa)	LCP2	3937	3
FYN binding protein (FYB-120/130)	FYB	2533	3
Spleen tyrosine kinase	SYK	6850	3
major histocompatibility complex, class II, DP alpha 1	HLA-DPA1	3113	3
CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)	CD74	972	3
CD180 antigen	CD180	4064	3
class II, major histocompatibility complex, transactivator	CIITA	4261	3
B-cell linker	BLNK	29760	3
interferon regulatory factor 8 ; interferon regulatory factor 8	IRF8	3394	3
interleukin 18 (interferon-gamma-inducing factor)	IL18	3606	3
interleukin 12 receptor, beta 1	IL12RB1	3594	3
lysozyme (renal amyloidosis)	LYZ ; LILRB1	10859	3
Lymphocyte cytosolic protein 2 (SH2 domain containing leukocyte protein of 76kDa)	LCP2	3937	3
CD3E antigen, epsilon polypeptide (TiT3 complex)	CD3E	916	3
C-type lectin domain family 2, member D	CLEC2D	29121	3
dipeptidylpeptidase 4 (CD26, adenosine deaminase complexing protein 2)	DPP4	1803	3
transcription factor 7 (T-cell specific, HMG-box)	TCF7	6932	3
Tumor necrosis factor (ligand) superfamily, member 8	TNFSF8	944	3
cytotoxic T-lymphocyte-associated protein 4	CTLA4	1493	3
cold autoinflammatory syndrome 1	CIAS1	114548	3
killer cell lectin-like receptor subfamily C, member 4 ; killer cell lectin-like receptor subfamily K, member 1	KLRC4 ; KLRK1	22914	3
Arachidonate 5-lipoxygenase	ALOX5	240	3
killer cell lectin-like receptor subfamily K, member 1	KLRK1	22914	3

Appendix J: Inflammatory genes in AAA vs. NA (continued)

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
I factor (complement)	IF	3426	3
major histocompatibility complex, class II, DQ beta 1	HLA-DQB1	3119	3
major histocompatibility complex, class II, DO alpha	HLA-DOA	3111	3
trefoil factor 3 (intestinal)	TFF3	7033	3
CD53 antigen	CD53	963	3
major histocompatibility complex, class II, DM alpha	HLA-DMA	3108	3
CD1C antigen, c polypeptide	CD1C	911	3
platelet-activating factor receptor	PTAFR	5724	3
Immunoglobulin kappa variable 1-5	IGKC	3514	3
killer cell lectin-like receptor subfamily F, member 1	KLRF1	51348	3
CD79B antigen (immunoglobulin-associated beta)	CD79B	974	3
chemokine (C-C motif) receptor 2 ; chemokine (C-C motif) receptor 2	CCR2	1231	3
myeloid cell nuclear differentiation antigen ; myeloid cell nuclear differentiation antigen	MNDA	4332	3
ring finger protein 125	RNF125	54941	3
CD80 antigen (CD28 antigen ligand 1, B7-1 antigen)	CD80	941	3
G-protein signalling modulator 3 (AGS3-like, C. elegans)	GPSM3	63940	3
C-type lectin domain family 4, member A	CLEC4A	50856	3
tumor necrosis factor (ligand) superfamily, member 4 (tax-transcriptionally activated glycoprotein 1, 34kDa)	TNFSF4	7292	3
guanylate binding protein 4	GBP4	115361	3
leukocyte specific transcript 1	LST1	7940	3
sema domain, immunoglobulin domain (Ig), transmembrane domain (TM)	SEMA4D	10507	2
prostaglandin E receptor 4 (subtype EP4)	PTGER4	5734	2
Decay accelerating factor for complement (CD55, Cromer blood group system)	DAF	1604	2
interleukin 1, beta	IL1B	3553	2
Arachidonate 5-lipoxygenase	ALOX5	240	2

Appendix J: Inflammatory genes in AAA vs. NA (continued)

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
CD1D antigen, d polypeptide ; CD1D antigen, d polypeptide	CD1D	912	2
CD84 antigen (leukocyte antigen)	CD84	8832	2
leukocyte specific transcript 1	LST1	7940	2
phosphoprotein associated with glycosphingolipid microdomains 1	PAG1	55824	2
Annexin A1	ANXA1	301	2
chemokine (C-X3-C motif) receptor 1	CX3CR1	1524	2
integrin, alpha L (antigen CD11A (p180), lymphocyte function-associated antigen 1; alpha polypeptide)	ITGAL	3683	2
leukocyte specific transcript 1	LST1	7940	2
CD86 antigen (CD28 antigen ligand 2, B7-2 antigen)	CD86	942	2
toll-like receptor 1	TLR1	7096	2
leukocyte specific transcript 1	LST1	7940	2
matrix metallopeptidase 25	MMP25	64386	2
Interleukin 24	IL24	11009	2
interleukin 6 receptor ; interleukin 6 receptor	IL6R	3570	2
allograft inflammatory factor 1	AIF1	199	2
major histocompatibility complex, class II, DR alpha	HLA-DRA	3122	2
nucleotide-binding oligomerization domains 27	NOD27	84166	2
ectodysplasin A	EDA	1896	2
tumor necrosis factor (ligand) superfamily, member 7	TNFSF7	970	2
major histocompatibility complex, class I, C	HLA-C	3107	2
chemokine (C motif) ligand 1 ; chemokine (C motif) ligand 2	XCL1 ; XCL2	6375	2

Appendix J: Inflammatory genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold Change
clusterin	CLU	1191	6
ADAM metallopeptidase domain 33	ADAM33	80332	5
chemokine (C-X3-C motif) ligand 1	CX3CL1	6376	4
histone deacetylase 9	HDAC9	9734	4
amine oxidase, copper containing 3 (vascular adhesion protein 1)	AOC3	8639	4
histamine receptor H1	HRH1	3269	4
parathymosin	PTMS	5763	4
transcription elongation factor A (SII), 3	TCEA3	6920	3
GTP binding protein overexpressed in skeletal muscle	GEM	2669	3
CD27-binding (Siva) protein	SIVA	10572	3
transcription elongation factor A (SII), 2	TCEA2	6919	3
mannan-binding lectin serine peptidase 1 (C4/C2 activating component of Ra-reactive factor)	MASP1	5648	3
histone deacetylase 5	HDAC5	10014	3
toll interacting protein	TOLLIP	54472	3
integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	ITGB1	3688	3
barrier to autointegration factor 1	BANF1	8815	3
protein kinase, interferon-inducible double stranded RNA dependent activator	PRKRA	8575	3
fusion (involved in t(12;16) in malignant liposarcoma)	FUS	2521	3
integrin, beta 1 (fibronectin receptor, beta polypeptide, antigen CD29 includes MDF2, MSK12)	ITGB1	3688	3
histone deacetylase 7A	HDAC7A	51564	2
microsomal glutathione S-transferase 3	MGST3	4259	2
Microtubule-associated protein, RP/EB family, member 2	MAPRE2	10982	2
transforming growth factor, beta 1 (Camurati-Engelmann disease)	TGFB1	7040	2
nuclear factor (erythroid-derived 2)-like 1	NFE2L1	4779	2
myeloid leukemia factor 2	MLF2	8079	2

Appendix J: Inflammatory genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold Change
CD27-binding (Siva) protein	SIVA	10572	2
vacuolar protein sorting 45A (yeast)	VPS45A	11311	2
IK cytokine, down-regulator of HLA II ; IK cytokine, down-regulator of HLA II	IK	3550	2
toll interacting protein	TOLLIP	54472	2
eukaryotic translation initiation factor 2B, subunit 3 gamma, 58kDa	EIF2B3	8891	2
Interleukin 17D	IL17D	53342	2
zinc finger protein 161	ZNF161	7716	2
annexin A11	ANXA11	311	2
inter-alpha (globulin) inhibitor H4 (plasma Kallikrein-sensitive glycoprotein)	ITIH4	3700	2
tetraspanin 9	TSPAN9	10867	2
ankyrin repeat and SOCS box-containing 1	ASB1	51665	2
hypothetical protein FLJ21148	FLJ21148	79918	2
nuclear factor (erythroid-derived 2)-like 1	NFE2L1	4779	2
signal transducer and activator of transcription 3 (acute-phase response factor)	STAT3	6774	2
TIA1 cytotoxic granule-associated RNA binding protein-like 1	TIAL1	7073	2
nuclear factor (erythroid-derived 2)-like 1	NFE2L1	4779	2
cytochrome P450, family 26, subfamily B, polypeptide 1	CYP26B1	56603	2
histone deacetylase 4	HDAC4	9759	2
tetraspanin 9 ; tetraspanin 9	TSPAN9	10867	2
ankyrin repeat and SOCS box-containing 1	ASB1	51665	2
sequestosome 1	SQSTM1	8878	2
sterile alpha and TIR motif containing 1	SARM1	23098	2
interferon induced transmembrane protein 2 (1-8D)	IFITM2	10581	2

Appendix K: Proteolytic genes in AAA vs.NA

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
carboxypeptidase Z ; carboxypeptidase Z	CPZ	8532	12
tumor necrosis factor receptor superfamily, member 7	TNFRSF7	939	11
CD3G antigen, gamma polypeptide (TiT3 complex)	CD3G	917	9
heparan sulfate (glucosamine) 3-O-sulfotransferase 3B1	HS3ST3B1	9953	9
granzyme B (granzyme 2, cytotoxic T-lymphocyte-associated serine esterase 1)	GZMB	3002	8
matrix metallopeptidase 9 (gelatinase B, 92kDa gelatinase, 92kDa type IV collagenase)	MMP9	4318	8
Ankyrin repeat and KH domain containing 1	ANKHD1	54882	8
matrix-remodelling associated 5	MXRA5	25878	8
cathepsin S	CTSS	1520	7
tumor necrosis factor, alpha-induced protein 3	TNFAIP3	7128	6
calcium/calmodulin-dependent protein kinase IV	CAMK4	814	5
zeta-chain (TCR) associated protein kinase 70kDa	ZAP70	7535	5
ADAM metallopeptidase domain 28	ADAM28	10863	5
interleukin 2 receptor, gamma (severe combined immunodeficiency)	IL2RG	3561	5
protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	PTPN22	26191	5
serine/threonine kinase 4	STK4	6789	5
lymphocyte-specific protein tyrosine kinase	LCK	3932	5
FK506 binding protein 11, 19 kDa	FKBP11	51303	5
tumor necrosis factor, alpha-induced protein 3	TNFAIP3	7128	5
dual adaptor of phosphotyrosine and 3-phosphoinositides	DAPP1	27071	5
ST8 alpha-N-acetyl-neuraminide alpha-2,8-sialyltransferase 4	ST8SIA4	7903	5
CD3D antigen, delta polypeptide (TiT3 complex)	CD3D	915	5
protein tyrosine phosphatase, receptor type, C	PTPRC	5788	4
Serine/threonine kinase 17b (apoptosis-inducing)	STK17B	9262	4
IL2-inducible T-cell kinase	ITK	3702	4

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
carboxypeptidase M	CPM	1368	4
dipeptidylpeptidase 4 (CD26, adenosine deaminase complexing protein 2)	DPP4	1803	4
Matrix-metallopeptidase 3	MMP-3	4314	4
protein tyrosine phosphatase, receptor type, C	PTPRC	5788	4
FYN oncogene related to SRC, FGR, YES	FYN	2534	4
type 1 tumor necrosis factor receptor shedding aminopeptidase regulator	ARTS-1	51752	4
protein tyrosine phosphatase, receptor type, C	PTPRC	5788	4
Doublecortin and CaM kinase-like 1	DCAMKL1	9201	4
protein tyrosine phosphatase, non-receptor type 22 (lymphoid)	PTPN22	26191	4
Protein kinase C, beta 1	PRKCB1	5579	4
protein phosphatase 2, regulatory subunit B (B56), gamma isoform	PPP2R5C	5527	4
serine/threonine kinase 17b (apoptosis-inducing)	STK17B	9262	4
chromosome 11 open reading frame 17	C11orf17	56672	4
SNF1-like kinase 2	SNF1LK2	23235	3
lymphocyte-specific protein tyrosine kinase	LCK	3932	3
UDP-Gal:betaGlcNAc beta 1,3-galactosyltransferase, polypeptide 2	B3GALT2	8707	3
FYN binding protein (FYB-120/130)	FYB	2533	3
Spleen tyrosine kinase	SYK	6850	3
CD74 antigen (invariant polypeptide of major histocompatibility complex, class II antigen-associated)	CD74	972	3
corin, serine peptidase	CORIN	10699	3
interleukin 18 (interferon-gamma-inducing factor)	IL18	3606	3
Slingshot homolog 2 (Drosophila)	SSH2	85464	3
protein kinase C, beta 1	PRKCB1	5579	3
ring finger protein 141	RNF141	50862	3
CD3E antigen, epsilon polypeptide (TiT3 complex)	CD3E	916	3
caspase 1, apoptosis-related cysteine peptidase (interleukin 1, beta, convertase)	CASP1	114769	3
serum/glucocorticoid regulated kinase	SGK	6446	3

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
dipeptidylpeptidase 4 (CD26, adenosine deaminase complexing protein 2)	DPP4	1803	3
protein kinase, cAMP-dependent, regulatory, type I, alpha (tissue specific extinguisher 1)	PRKAR1A	5573	3
Protein kinase C, eta	PRKCH	5583	3
fms-related tyrosine kinase 3	FLT3	2322	3
Membrane-associated ring finger (C3HC4) 1	MARCH-I	55016	3
I factor (complement)	IF	3426	3
Ubiquitin specific peptidase 3	USP3	9960	3
napsin B aspartic peptidase pseudogene	NAPSB	256236	3
caspase 10, apoptosis-related cysteine peptidase	CASP10	843	3
corin, serine peptidase	CORIN	10699	3
Bruton agammaglobulinemia tyrosine kinase	BTK	695	3
Membrane-associated ring finger (C3HC4) 1	MARCH-I	55016	3
similar to aspartate beta hydroxylase (ASPH)	LOC57168	57168	3
protein kinase C, theta	PRKCQ	5588	3
protein tyrosine phosphatase, non-receptor type 7	PTPN7	5778	3
A kinase (PRKA) anchor protein (yotiao) 9	AKAP9	10142	3
Death-associated protein kinase 1	DAPK1	1612	3
mitogen-activated protein kinase kinase 6	MAP2K6	5608	3
cathepsin H	CTSH	1512	3
carboxypeptidase M	CPM	1368	3
membrane-associated ring finger (C3HC4) 1	Mar-01	55016	3
PCTAIRE protein kinase 2	PCTK2	5128	3
RNA binding motif, single stranded interacting protein 1	IRAK3	11213	3
Matrilin 1, cartilage matrix protein	MATN1	4146	3
ring finger protein 125	RNF125	54941	3
CD80 antigen (CD28 antigen ligand 1, B7-1 antigen)	CD80	941	3

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
Protein tyrosine phosphatase, non-receptor type 1	PTPN1	5770	3
Ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast)	UBE2J1	51465	2
cathepsin K (pycnodysostosis)	CTSK	1513	2
myotubularin 1	MTM1	4534	2
mitogen-activated protein kinase kinase kinase 8	MAP3K8	1326	2
Rap guanine nucleotide exchange factor (GEF) 4	RAPGEF4	11069	2
caspase 8, apoptosis-related cysteine peptidase	CASP8	841	2
Slingshot homolog 2 (Drosophila)	SSH2	85464	2
Serine/threonine kinase 38	STK38	11329	2
disabled homolog 1 (Drosophila) ; OMA1 homolog, zinc metallopeptidase (S. cerevisiae)	DAB1	115209	2
activin A receptor, type IC	ACVR1C	130399	2
Mannosyl (alpha-1,3-)-glycoprotein beta-1,4-N-acetylglucosaminyltransferase, isoenzyme A	MGAT4A	11320	2
CDC14 cell division cycle 14 homolog A (S. cerevisiae)	CDC14A	8556	2
kinetochore associated 1	KNTC1	9735	2
DnaJ (Hsp40) homolog, subfamily B, member 9	DNAJB9	4189	2
CD86 antigen (CD28 antigen ligand 2, B7-2 antigen)	CD86	942	2
homocysteine-inducible, endoplasmic reticulum stress-inducible, ubiquitin-like domain member 1	HERPUD1	9709	2
toll-like receptor 1	TLR1	7096	2
RAB6 interacting protein 2	RAB6IP2	23085	2
Eukaryotic translation initiation factor 5	EIF5	1983	2
matrix metallopeptidase 25	MMP25	64386	2
ribosomal protein L7	RPL7	388401	2
proprotein convertase subtilisin/kexin type 6	PCSK6	5046	2
F-box and WD-40 domain protein 7 (archipelago homolog, Drosophila)	FBXW7	55294	2
baculoviral IAP repeat-containing 3	BIRC3	330	2

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
protein kinase, X-linked	PRKX	5613	2
abhydrolase domain containing 7	ABHD7	253152	2
ubiquitin-conjugating enzyme E2, J1 (UBC6 homolog, yeast)	UBE2J1	51465	2
BMP2 inducible kinase	BMP2K	55589	2
scavenger receptor class F, member 1	SCARF1	8578	2
Ubiquitin-like domain containing CTD phosphatase 1	MGC10067	134510	2
fucosyltransferase 8 (alpha (1,6) fucosyltransferase)	FUT8	2530	2

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
aortic preferentially expressed gene 1	APEG1	10290	56
ADAM metallopeptidase with thrombospondin type 1 motif, 8	ADAMTS8	11095	15
receptor-interacting serine-threonine kinase 4	RIPK4	54101	13
neurotrophic tyrosine kinase, receptor, type 3	NTRK3	4916	11
caspase 12 pseudogene 1	CASP12P1	120329	9
Proprotein convertase subtilisin/kexin type 7	PCSK7	9159	9
PDZ domain containing RING finger 3	PDZRN3	23024	7
ligand of numb-protein X	LNX	84708	6
supervillin	SVIL	6840	6
chromosome 9 open reading frame 3	C9orf3	84909	6
V-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	ERBB4	2066	6
protease, serine, 35	PRSS35	167681	5
ring finger and FYVE-like domain containing 1	RFFL	117584	5
protein tyrosine phosphatase, non-receptor type 21	PTPN21	11099	5
calcium/calmodulin-dependent protein kinase (CaM kinase) II gamma	CAMK2G	818	5
erythrocyte membrane protein band 4.9 (dematin)	EPB49	2039	5
Mitochondrial ribosomal protein S6	MRPS6	64968	5
lecithin-cholesterol acyltransferase	LCAT	3931	5
ADAM metallopeptidase domain 33	ADAM33	80332	5
integrin-linked kinase	ILK	3611	4
chromosome 1 open reading frame 24	C1orf24	116496	4
tubulin tyrosine ligase-like family, member 7	TTLL7	79739	4
heat shock 27kDa protein 1	HSPB1	3315	4
cullin-associated and neddylation-dissociated 2 (putative)	CAND2	23066	4
Bone morphogenetic protein receptor, type IB	BMPR1B	658	4
methionine sulfoxide reductase B3	MSRB3	253827	4
nucleosome assembly protein 1-like 3	NAP1L3	4675	4

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
F-box and leucine-rich repeat protein 19	FBXL19	54620	4
transducin (beta)-like 1X-linked	TBL1X	6907	4
transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)	TGM2	7052	4
protein tyrosine phosphatase, receptor type, G	PTPRG	5793	4
ankyrin repeat and BTB (POZ) domain containing 2	ABTB2	25841	4
adaptor-related protein complex 2, alpha 1 subunit	AP2A1	160	4
CDC14 cell division cycle 14 homolog B (S. cerevisiae)	CDC14B	8555	4
OTU domain, ubiquitin aldehyde binding 2	OTUB2	78990	4
mitogen-activated protein kinase kinase 7	MAP2K7	5609	4
ADAM metallopeptidase with thrombospondin type 1 motif, 9	ADAMTS9	56999	4
protein phosphatase 2A, regulatory subunit B' (PR 53)	PPP2R4	5524	4
myosin, light polypeptide kinase ; myosin, light polypeptide kinase	MYLK	4638	4
chromosome 1 open reading frame 24	C1orf24	116496	4
v-ets erythroblastosis virus E26 oncogene like (avian)	ERG	2078	4
heat shock 70kDa protein 2	HSPA2	3306	4
V-erb-a erythroblastic leukemia viral oncogene homolog 4 (avian)	ERBB4	2066	4
G protein-coupled receptor kinase 5	GRK5	2869	3
membrane protein, palmitoylated 6 (MAGUK p55 subfamily member 6)	MPP6	51678	3
Endothelin converting enzyme 1	ECE1	1889	3
ADAM metallopeptidase with thrombospondin type 1 motif, 15	ADAMTS15	170689	3
methionine sulfoxide reductase B2	MSRB2	22921	3
v-src sarcoma (Schmidt-Ruppin A-2) viral oncogene homolog (avian)	SRC	6714	3
natriuretic peptide receptor B/guanylate cyclase B (atrionatriuretic peptide receptor B)	NPR2	4882	3
actin related protein 2/3 complex, subunit 4, 20kDa	ARPC4	10093	3
matrix metallopeptidase 16 (membrane-inserted)	MMP16	4325	3
carbohydrate (chondroitin 6) sulfotransferase 3	CHST3	9469	3

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
rho/rac guanine nucleotide exchange factor (GEF) 2	ARHGEF2	9181	3
peptidylglycine alpha-amidating monooxygenase	PAM	5066	3
guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	3
Protein tyrosine phosphatase-like (proline instead of catalytic arginine), member a	PTPLA	9200	3
adaptor-related protein complex 2, alpha 1 subunit	AP2A1	160	3
tripartite motif-containing 47	TRIM47	91107	3
guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	3
methionyl aminopeptidase 1	METAP1	23173	3
transducin (beta)-like 1X-linked	TBL1X	6907	3
transglutaminase 2 (C polypeptide, protein-glutamine-gamma-glutamyltransferase)	TGM2	7052	3
Insulin-like growth factor 1 receptor	IGF1R	3480	3
protein tyrosine phosphatase, non-receptor type 3	PTPN3	5774	3
platelet derived growth factor D	PDGFD	80310	3
lysyl-tRNA synthetase	KARS	3735	3
HIV-1 Tat interacting protein, 60kDa	HTATIP	10524	3
heat shock 27kDa protein 2	HSPB2	3316	3
Epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	EGFR	1956	3
protein tyrosine phosphatase, receptor type, D	PTPRD	5789	3
microtubule-associated protein 1 light chain 3 alpha	MAP1LC3A	84557	3
WNK lysine deficient protein kinase 3	WNK3	65267	3
VAMP (vesicle-associated membrane protein)-associated protein B and C	VAPB	9217	3
ribonuclease, RNase A family, 4	RNASE4	6038	3
Supervillin	SVIL	6840	3
tubulin, beta 3	TUBB3	10381	3
discoidin domain receptor family, member 1	DDR1	780	3
Bone morphogenetic protein receptor, type IB	BMPR1B	658	3

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
mitochondrial ribosomal protein L21	MRPL21	219927	3
dual specificity phosphatase 19	DUSP19	142679	3
beta-site APP-cleaving enzyme 1	BACE1	23621	3
myotubularin related protein 2	MTMR2	8898	3
amyloid beta (A4) precursor protein-binding, family B, member 1 (Fe65)	APBB1	322	3
tubulin, beta polypeptide	TUBB	203068	3
mitogen-activated protein kinase kinase kinase 6	MAP3K6	9064	3
microtubule associated serine/threonine kinase family member 4	MAST4	23227	3
nuclear protein localization 4	NPL4	55666	3
v-ets erythroblastosis virus E26 oncogene like (avian)	ERG	2078	3
EPH receptor A4	EPHA4	2043	3
Protein tyrosine phosphatase, non-receptor type 23	PTPN23	25930	3
protein kinase, cAMP-dependent, regulatory, type II, alpha	PRKAR2A	5576	3
ST6 (alpha-N-acetyl-neuraminyl-2,3-beta-galactosyl-1,3)	ST6GALNAC6	30815	3
UDP-N-acetyl-alpha-D-galactosamine:polypeptide N-acetylgalactosaminyltransferase 2 (GalNAc-T2)	GALNT2	2590	3
Membrane protein, palmitoylated 6 (MAGUK p55 subfamily member 6)	MPP6	51678	3
Cyclin-dependent kinase 8	CDK8	1024	3
ATP-binding cassette, sub-family C (CFTR/MRP), member 1	ABCC1	4363	2
calpain 5	CAPN5	726	2
protein tyrosine phosphatase, non-receptor type 11 (Noonan syndrome 1)	PTPN11	5781	2
epidermal growth factor receptor (erythroblastic leukemia viral (v-erb-b) oncogene homolog, avian)	EGFR	1956	2
COX11 homolog, cytochrome c oxidase assembly protein (yeast)	COX11	1353	2
dystroglycan 1 (dystrophin-associated glycoprotein 1)	DAG1	1605	2
SCY1-like 1 (S. cerevisiae)	SCYL1	57410	2
TRIO and F-actin binding protein	TRIOBP	11078	2
chaperonin containing TCP1, subunit 7 (eta)	CCT7	10574	2

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
laminin, gamma 1 (formerly LAMB2)	LAMC1	3915	2
cytoskeleton associated protein 1	CKAP1	1155	2
ring finger protein 150	RNF150	57484	2
MAP/microtubule affinity-regulating kinase 1	MARK1	4139	2
myosin regulatory light chain interacting protein	MYLIP	29116	2
Chromosome 9 open reading frame 3	C9orf3	84909	2
H2A histone family, member J	H2AFJ	55766	2
Tight junction protein 1 (zona occludens 1)	TJP1	7082	2
ubiquitin-conjugating enzyme E2M (UBC12 homolog, yeast)	UBE2M	9040	2
v-akt murine thymoma viral oncogene homolog 2	AKT2	208	2
pregnancy-associated plasma protein A, pappalysin 1	PAPPA	5069	2
hypothetical protein MGC2744	MGC2744	80755	2
Exostoses (multiple) 1	EXT1	2131	2
pyruvate dehydrogenase kinase, isoenzyme 2	PDK2	5164	2
ring finger protein 180	RNF180	285671	2
tripartite motif-containing 28	TRIM28	10155	2
eukaryotic translation initiation factor 4E	EIF4E	1977	2
spectrin, alpha, non-erythrocytic 1 (alpha-fodrin)	SPTAN1	6709	2
prolyl endopeptidase-like	PREPL	9581	2
histidyl-tRNA synthetase-like	HARSL	23438	2
prefoldin 1	PFDN1	5201	2
Pelota homolog (Drosophila)	PELO	53918	2
leucine rich repeat containing 41	LRRC41	10489	2
ST3 beta-galactoside alpha-2,3-sialyltransferase 3	ST3GAL3	6487	2
guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	2

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
BRCA1 associated RING domain 1	BARD1	580	2
ring finger protein 25	RNF25	64320	2
CDC42 binding protein kinase alpha (DMPK-like)	CDC42BPA	8476	2
low density lipoprotein receptor-related protein 8, apolipoprotein e receptor	LRP8	7804	2
N-myristoyltransferase 1	NMT1	4836	2
Zinc finger, A20 domain containing 1	ZA20D1	56957	2
ribosomal protein L39-like	RPL39L	116832	2
DEAD (Asp-Glu-Ala-Asp) box polypeptide 1	DDX1	1653	2
arginyl-tRNA synthetase	RARS	5917	2
ubiquitin specific peptidase 20	USP20	10868	2
H2A histone family, member J	H2AFJ	55766	2
Protein tyrosine phosphatase, receptor type, D	PTPRD	5789	2
RNA binding motif protein 9	RBM9	23543	2
calcium/calmodulin-dependent protein kinase (CaM kinase) II delta	CAMK2D	817	2
TRAF2 and NCK interacting kinase	TNIK	23043	2
neural precursor cell expressed, developmentally down-regulated 4	NEDD4	4734	2
zinc metallopeptidase (STE24 homolog, yeast)	ZMPSTE24	10269	2
eukaryotic translation initiation factor 4 gamma, 1	EIF4G1	1981	2
Heat shock 70kDa protein 4	HSPA4	3308	2
nucleosome assembly protein 1-like 5	NAP1L5	266812	2
cytoskeleton associated protein 1	CKAP1	1155	2
ribosomal protein S27-like	RPS27L	51065	2
Janus kinase 2 (a protein tyrosine kinase)	JAK2	3717	2
proliferation-associated 2G4, 38kDa	PA2G4	5036	2
C-terminal binding protein 1	CTBP1	1487	2

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
Protein tyrosine phosphatase, receptor type, D	PTPRD	5789	2
HMT1 hnRNP methyltransferase-like 1 (S. cerevisiae)	HRMT1L1	3275	2
mitogen-activated protein kinase kinase kinase 5	MAP3K5	4217	2
tubulin, beta 2	TUBB2	7280	2
casein kinase 2, alpha prime polypeptide	CSNK2A2	1459	2
v-ets erythroblastosis virus E26 oncogene like (avian) ; v-ets erythroblastosis virus E26 oncogene like (avian)	ERG	2078	2
C-terminal binding protein 1	CTBP1	1487	2
cysteinyl-tRNA synthetase	CARS	833	2
discoidin domain receptor family, member 1	DDR1	780	2
par-3 partitioning defective 3 homolog (C. elegans)	PARD3	56288	2
AHA1, activator of heat shock 90kDa protein ATPase homolog 1 (yeast)	AHSA1	10598	2
prefoldin 2	PFDN2	5202	2
protein phosphatase 2 (formerly 2A), catalytic subunit, beta isoform	PPP2CB	5516	2
retinoic acid receptor, alpha ; retinoic acid receptor, alpha	RARA	5914	2
sterile alpha motif and leucine zipper containing kinase AZK	ZAK	51776	2
guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	2
fyn-related kinase	FRK	2444	2
ubiquitin specific peptidase 47	USP47	55031	2
NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 13	NDUFA13	51079	2
Discoidin domain receptor family, member 2	DDR2	4921	2
protein inhibitor of activated STAT, 3	PIAS3	10401	2
vesicle-associated membrane protein 4	VAMP4	8674	2
uronyl-2-sulfotransferase	UST	10090	2
ubiquitin-conjugating enzyme E2G 2 (UBC7 homolog, yeast)	UBE2G2	7327	2
S-phase kinase-associated protein 1A (p19A)	SKP1A	6500	2
ubiquitination factor E4B (UFD2 homolog, yeast)	UBE4B	10277	2

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
carboxypeptidase X (M14 family), member 2	CPXM2	119587	2
MID1 interacting protein 1 (gastrulation specific G12-like (zebrafish))	MID1IP1	58526	2
histone deacetylase 8	HDAC8	55869	2
mitochondrial ribosomal protein L33	MRPL33	9553	2
Supervillin	SVIL	6840	2
F-box and WD-40 domain protein 4	FBXW4	6468	2
ring finger protein 180	RNF180	285671	2
mitochondrial ribosomal protein L4	MRPL4	51073	2
methionine sulfoxide reductase B2	MSRB2	22921	2
suppressor of Ty 16 homolog (S. cerevisiae)	SUPT16H	11198	2
Eukaryotic translation initiation factor 2C, 2	EIF2C2	27161	2
Lemur tyrosine kinase 2	LMTK2	22853	2
prenylcysteine oxidase 1	PCYOX1	51449	2
ubiquitin specific peptidase 21	USP21	27005	2
isoprenylcysteine carboxyl methyltransferase	ICMT	23463	2
gelsolin (amyloidosis, Finnish type)	GSN	2934	2
mitogen-activated protein kinase kinase kinase 3	MAP3K3	4215	2
glutaredoxin 2	GLRX2	51022	2
ribosomal protein S23	RPS23	6228	2
ubiquitin specific peptidase 47	USP47	55031	2
ADAM metallopeptidase with thrombospondin type 1 motif, 3	ADAMTS3	9508	2
H2A histone family, member V	H2AFV	94239	2
mitochondrial ribosomal protein S18C	MRPS18C	51023	2
tripartite motif-containing 56	TRIM56	81844	2
BRCA1 associated protein	BRAP	8315	2
dual specificity phosphatase 19	DUSP19	142679	2

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
pelota homolog (Drosophila)	PELO	53918	2
ubiquitin specific peptidase 31	USP31	57478	2
DnaJ (Hsp40) homolog, subfamily C, member 8	DNAJC8	22826	2
alpha-2-macroglobulin	A2M	2	2
family with sequence similarity 80, member B	FAM80B	57494	2
myosin regulatory light chain interacting protein	MYLIP	29116	2
splicing factor, arginine/serine-rich 8 (suppressor-of-white-apricot homolog, Drosophila)	SFRS8	6433	2
Calcium/calmodulin-dependent protein kinase (CaM kinase) II gamma	CAMK2G	818	2
serine/threonine kinase 19	STK19	8859	2
gap junction protein, alpha 4, 37kDa (connexin 37)	GJA4	2701	2
discoidin domain receptor family, member 2	DDR2	4921	2
prolyl endopeptidase-like	PREPL	9581	2
superkiller viralicidic activity 2-like (S. cerevisiae)	SKIV2L	6499	2
zinc finger, CSL-type containing 2	ZCSL2	285381	2
actinin, alpha 2	ACTN2	88	2
F-box and leucine-rich repeat protein 7	FBXL7	23194	2
methyltransferase like 5	METTL5	29081	2
serine/threonine kinase 17a (apoptosis-inducing)	STK17A	9263	2
guanine nucleotide binding protein (G protein), alpha 11 (Gq class)	GNA11	2767	2
ubiquitin-conjugating enzyme E2G 2 (UBC7 homolog, yeast)	UBE2G2	30851	2
bone morphogenetic protein receptor, type II (serine/threonine kinase)	BMPR2	659	2
selenocysteine lyase ; NEDD8-conjugating enzyme	SCLY	140739	2
cyclin-dependent kinase 9 (CDC2-related kinase)	CDK9	1025	2
F-box protein 9	FBXO9	26268	2
dystroglycan 1 (dystrophin-associated glycoprotein 1)	DAG1	1605	2
glycophorin C (Gerbich blood group)	GYPC	2995	2

Appendix K: Proteolytic genes in AAA vs. NA (continued)

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
protein phosphatase 1G (formerly 2C), magnesium-dependent, gamma isoform	PPM1G	5496	2
mitogen-activated protein kinase 7	MAPK7	5598	2
ubiquitin specific peptidase 47	USP47	55031	2
HLA-B associated transcript 3	BAT3	7917	2
mitogen-activated protein kinase kinase kinase 4	MAP3K4	4216	2
SREBP cleavage-activating protein	SCAP	22937	2
chaperonin containing TCP1, subunit 5 (epsilon)	CCT5	22948	2
rho/rac guanine nucleotide exchange factor (GEF) 2	ARHGEF2	9181	2
chromosome 20 open reading frame 14	C20orf14	24148	2
protein phosphatase methylesterase-1	PME-1	51400	2
heat shock 10kDa protein 1 (chaperonin 10)	HSPE1	3336	2
retinoblastoma-associated factor 600	RBAF600	23352	2
ubiquitin protein ligase E3C	UBE3C	9690	2
slingshot homolog 3 (Drosophila)	SSH3	54961	2
surfeit 6	SURF6	6838	2
F-box protein 42	FBXO42	54455	2
ubiquitin-conjugating enzyme E2L 3	UBE2L3	7332	2
protein tyrosine phosphatase, receptor type, K	PTPRK	5796	2
EPH receptor A4	EPHA4	2043	2
chaperonin containing TCP1, subunit 3 (gamma)	CCT3	7203	2

Appendix L: Apoptotic genes in AAA vs. NA.

Upregulated genes	Gene symbol	Entrez Gene ID	Fold change
SLAM family member 7	SLAMF7	57823	19
Fas apoptotic inhibitory molecule 3	FAIM3	9214	13
tumor necrosis factor receptor superfamily, member 7	TNFRSF7	939	11
CD38 antigen (p45)	CD38	952	10
CD3G antigen, gamma polypeptide (TiT3 complex)	CD3G	917	9
tumor necrosis factor, alpha-induced protein 3	TNFAIP3	7128	6
serine/threonine kinase 4	STK4	6789	5
Serine/threonine kinase 17b (apoptosis-inducing)	STK17B	9262	4
BCL2-like 11 (apoptosis facilitator)	BCL2L11	10018	4
tumor protein p53 inducible nuclear protein 1	TP53INP1	94241	4
CD74 antigen	CD74	972	3
interleukin 18 (interferon-gamma-inducing factor)	IL18	3606	3
caspase 1, apoptosis-related cysteine peptidase (interleukin 1, beta, convertase)	CASP1	114769	3
Tumor necrosis factor (ligand) superfamily, member 8	TNFSF8	944	3
BCL2-like 11 (apoptosis facilitator)	BCL2L11	10018	3
caspase 10, apoptosis-related cysteine peptidase	CASP10	843	3
Death-associated protein kinase 1	DAPK1	1612	3
tumor necrosis factor receptor superfamily, member 18	TNFRSF18	8784	3
interleukin 1, beta	IL1B	3553	2
caspase 8, apoptosis-related cysteine peptidase	CASP8	841	2
activin A receptor, type IC	ACVR1C	130399	2
deoxyribonuclease I-like 3	DNASE1L3	1776	2
Interleukin 24	IL24	11009	2
TIMP metallopeptidase inhibitor 3 (Sorsby fundus dystrophy, pseudoinflammatory)	TIMP3	7078	2

Appendix L: Apoptotic genes in AAA vs. NA (continued).

Downregulated genes	Gene symbol	Entrez Gene ID	Fold change
caspase 12 pseudogene 1	CASP12P1	120329	9
clusterin	CLU	1191	6
ring finger and FYVE-like domain containing 1	RFFL	117584	5
GULP, engulfment adaptor PTB domain containing 1	GULP1	51454	5
epithelial membrane protein 2	EMP2	2013	4
PRKC, apoptosis, WT1, regulator	PAWR	5074	3
BRCA1 associated RING domain 1	BARD1	580	3
B-cell receptor-associated protein 29	BCAP29	55973	3
serine/threonine kinase 17a (apoptosis-inducing)	STK17A	9263	3
B-cell receptor-associated protein 29	BCAP29	55973	3
Insulin-like growth factor 1 receptor	IGF1R	3480	3
BCL2-like 2	BCL2L2	599	3
tubulin, beta, 2	TUBB2	10383	3
cell division cycle 2-like 1 (PITSLRE proteins)	CDC2L1	984	3
BCL2-associated athanogene 3	BAG3	9531	3
tubulin, beta polypeptide ; tubulin, beta polypeptide	TUBB	203068	3
poly(rC) binding protein 4	PCBP4	57060	3
peroxiredoxin 2 ; peroxiredoxin 2	PRDX2	7001	3
B-cell receptor-associated protein 29	BCAP29	55973	3
eukaryotic translation elongation factor 1 epsilon 1	EEF1E1	9521	3
Death effector domain containing	DEDD	9191	2
nerve growth factor receptor (TNFRSF16) associated protein 1	NGFRAP1	27018	2
mitogen-activated protein kinase kinase kinase 5	MAP3K5	4217	2
CD27-binding (Siva) protein	SIVA	10572	2
protein phosphatase 2 (formerly 2A), catalytic subunit, beta isoform	PPP2CB	5516	2
sterile alpha motif and leucine zipper containing kinase AZK	ZAK	51776	2
NADH dehydrogenase (ubiquinone) 1 alpha subcomplex, 13	NDUFA13	51079	2

Appendix L: Apoptotic genes in AAA vs. NA (continued).

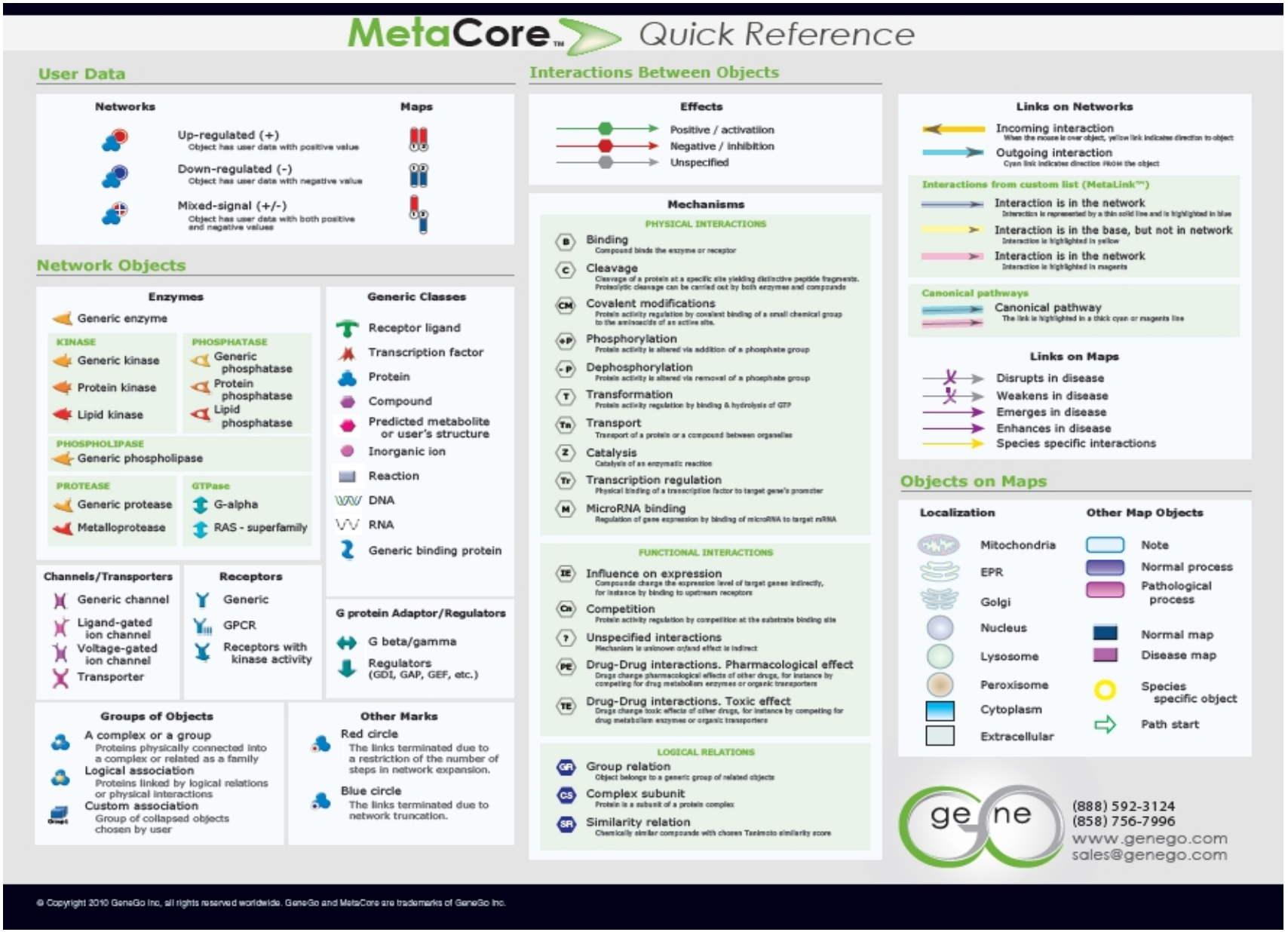
Downregulated genes	Gene symbol	Entrez Gene ID	Fold change
tumor protein p53 binding protein, 2	TP53BP2	7159	2
nucleolar protein 3 (apoptosis repressor with CARD domain)	NOL3	8996	2
death effector domain containing	DEDD	9191	2
glutaredoxin 2	GLRX2	51022	2
p8 protein (candidate of metastasis 1)	P8	26471	2
modulator of apoptosis 1	MOAP1	64112	2
cell division cycle 2-like 1 (PITSLRE proteins) ; cell division cycle 2-like 2 (PITSLRE proteins)	CDC2L1 ; CDC2L2	984 ; 985	2
Phosphatase and tensin homolog (mutated in multiple advanced cancers 1)	PTEN	5728	2
tetratricopeptide repeat domain 11	TTC11	51024	2
serine/threonine kinase 3 (STE20 homolog, yeast)	STK3	6788	2
apoptosis-inducing factor (AIF)-like mitochondrion-associated inducer of death	AMID	84883	2
MAP/microtubule affinity-regulating kinase 4	MARK4	57787	2
serine/threonine kinase 17a (apoptosis-inducing)	STK17A	9263	2
voltage-dependent anion channel 1	VDAC1	7416	2
Rabaptin, RAB GTPase binding effector protein 1	RABEP1	9135	2
fragile X mental retardation, autosomal homolog 1	FXR1	8087	2
mitogen-activated protein kinase kinase kinase 5	MAP3K5	4217	2
Protein phosphatase 2 (formerly 2A), catalytic subunit, alpha isoform	PPP2CA	5515	2
death associated transcription factor 1	DATF1	11083	2
cullin 2	CUL2	8453	2
BCL2-associated athanogene	BAG1	573	2
defender against cell death 1 ; defender against cell death 1	DAD1	1603	2
apoptosis, caspase activation inhibitor	AVEN	57099	2

Appendix M: Angiogenic genes in AAA vs. NA

Upregulated genes	Gene Symbol	Entrez Gene ID	Fold change
type 1 tumor necrosis factor receptor shedding aminopeptidase regulator	ARTS-1	51752	4
interleukin 18 (interferon-gamma-inducing factor)	IL18	3606	3
plexin domain containing 1	PLXDC1	57125	2
vascular endothelial growth factor C	VEGFC	7424	2

Downregulated genes	Gene Symbol	Entrez Gene ID	Fold change
fibroblast growth factor 1 (acidic)	FGF1	2246	4
endothelial PAS domain protein 1	EPAS1	2034	4
jagged 1 (Alagille syndrome)	JAG1	182	4
fibroblast growth factor 2 (basic)	FGF2	2247	3
laminin, alpha 5	LAMA5	3911	3
fibroblast growth factor 2 (basic)	FGF2	2247	3
v-erb-b2 erythroblastic leukemia viral oncogene homolog 2	ERBB2	2064	3
ribonuclease, RNase A family, 4	RNASE4	6038	3
c-fos induced growth factor (vascular endothelial growth factor D)	FIGF	2277	3
endothelial PAS domain protein 1	EPAS1	2034	2
angiogenin, ribonuclease, RNase A family, 5 ; ribonuclease, RNase A family, 4	ANG	283	2

Appendix N: Legends to pathways and networks



ADAMTS-9: QRT-PCR RAW DATA

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
1	32.8189	28.6413	27.1823		
	32.9848	28.4601	27.2361		
	32.9055	28.8244	27.1899		
	32.9031	**28.6419**	**27.2028**	**27.9224**	**4.9807**
2	33.2198	26.8973	24.2499		
	33.2646	27.0835	24.1576		
	33.2422	27.0738	24.2584		
	33.2422	**27.0182**	**24.2220**	**25.6201**	**7.6221**
3	32.4859	26.0773	24.3902		
	32.2759	26.0622	24.2711		
	32.4268	26.0640	24.2975		
	32.3962	**26.0678**	**24.3196**	**25.1937**	**7.2025**
4	32.7858	26.4507	25.0108		
	32.4434	26.3243	24.8534		
	32.2730	26.1930	24.8643		
	32.5007	**26.3227**	**24.9095**	**25.6161**	**6.8847**
5	32.1152	27.6957	25.6978		
	32.4574	27.4853	25.5027		
	32.1796	27.2469	25.5666		
	32.2507	**27.4760**	**25.5890**	**26.5325**	**5.7182**
6	34.4015	28.9730	26.9360		
	34.6654	29.0286	26.7803		
	34.9589	28.9822	27.0177		
	34.6753	**28.9946**	**26.9113**	**27.9530**	**6.7223**
7	33.0034	27.2454	25.5883		
	34.0062	27.2610	25.8369		
	31.4968	27.3853	26.0363		
	32.8355	**27.2972**	**25.8205**	**26.5589**	**6.2766**
8	32.6017	27.5042	26.1690		
	32.9769	27.4086	25.3954		
	33.8558	27.7803	25.3072		
	33.1448	**27.5644**	**25.6239**	**26.5941**	**6.5507**
9	33.5002	27.4201	25.2588		
	33.1599	27.6935	25.2095		
	33.4433	28.1190	25.4292		
	33.3678	**27.7442**	**25.2992**	**26.5217**	**6.8461**
10	33.7927	27.7750	25.7758		
	34.2142	27.6481	25.8295		
	34.3461	28.0045	25.6227		
	34.1177	**27.8092**	**25.7427**	**26.7759**	**7.3417**
11	33.1912	27.0128	25.3157		
	33.1282	27.0389	25.3994		
	32.6959	27.0723	25.3036		
	33.0051	**27.0413**	**25.3396**	**26.1905**	**6.8147**
12	31.1182	28.4114	26.2173		
	30.8246	28.3351	26.2152		
	30.7772	28.4564	26.1089		
	30.9067	**28.4010**	**26.1805**	**27.2907**	**3.6160**

ADAMTS-9: QRT-PCR RAW DATA (continued).

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
13	33.9345	28.0563	26.4304		
	33.2021	28.0156	26.3309		
	33.6546	28.0398	26.3394		
	33.5971	**28.0372**	**26.3669**	**27.2021**	**6.3950**

NA SAMPLES	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	32.3159	27.8676	26.0763		
	31.9773	27.7569	25.9361		
	32.1139	27.5515	25.8845		
	32.1357	**27.7253**	**25.9656**	**26.8455**	**5.2902**
2	29.6901	25.724	22.2915		
	29.5906	25.4896	22.353		
	29.6602	25.4302	22.2794		
	29.6470	**25.5479**	**22.30797**	**23.9280**	**5.7190**
3	33.2652	27.3042	26.7511		
	33.398	27.2492	26.229		
	33.2993	27.7063	26.0831		
	33.3208	**27.4199**	**26.3544**	**26.8872**	**6.4337**
4	31.6133	25.4673	23.6737		
	31.4052	25.7121	23.3977		
	31.7651	25.6252	23.5224		
	31.5945	**25.6015**	**23.5313**	**24.5664**	**7.0281**
5	32.7317	27.0188	24.6658		
	32.7947	27.0666	24.3919		
	33.2352	27.1001	24.4837		
	32.9205	**27.0618**	**24.5138**	**25.7878**	**7.1327**
6	33.1538	25.9239	24.1413		
	33.12	26.0085	24.0621		
	33.2273	26.3428	24.0428		
	33.1670	**26.0917**	**24.0821**	**25.0869**	**8.0801**
7	31.0439	24.6079	23.3357		
	31.0866	24.3444	23.2594		
	30.9574	24.5506	23.504		
	31.0293	**24.5010**	**23.3664**	**23.9337**	**7.0956**
8	31.5041	25.0378	22.8815		
	31.2687	25.0595	22.6917		
	31.1799	24.9753	22.62		
	31.3176	**25.0242**	**22.7311**	**23.8776**	**7.4399**

ADAMTS-9: QRT-PCR RAW DATA (continued).

AOD SAMPLE	C1	GAPDH C2	B actin C3	C4 = AVG (C2,C3)	C4-C1
1	33.8577	27.0771	25.1882		
	33.5836	27.0914	25.1698		
	33.3438	27.3594	24.5987		
	33.5950	**27.1760**	**24.9856**	**26.0808**	**7.5143**
2	31.6256	25.8524	23.9716		
	32.1118	25.809	23.6967		
	31.5994	25.7589	23.7727		
	31.7789	**25.8068**	**23.8137**	**24.8102**	**6.9687**
3	33.7426	26.9171	25.42		
	33.2318	27.0025	25.3802		
	33.4657	26.8578	25.1635		
	33.4800	**26.9258**	**25.3212**	**26.1235**	**7.3565**
4	34.4947	27.0749	25.4887		
	34.7854	26.9697	25.0513		
	34.5257	27.1162	25.3471		
	34.6019	**27.0536**	**25.2957**	**26.1747**	**8.4273**
5	35.1179	26.5472	24.6944		
	34.7619	26.4802	24.6038		
	34.625	26.384	24.4912		
	34.8349	**26.4705**	**24.5965**	**25.5335**	**9.3015**
6	31.6646	26.7261	25.0028		
	31.9271	26.7608	24.9524		
	31.4887	26.723	25.0537		
	31.6935	**26.7366**	**25.0030**	**25.8698**	**5.8237**
7	35.9478	27.0304	25.6261		
	35.1407	27.0908	25.5351		
	35.4576	27.0548	25.4895		
	35.5154	**27.0587**	**25.5502**	**26.3045**	**9.2109**
8	32.1039	25.8611	24.0096		
	31.9939	25.8855	24.0675		
	31.8308	25.8872	24.0054		
	31.9762	**25.8779**	**24.0275**	**24.9527**	**7.0235**
9	33.3406	28.2577	26.2222		
	33.1305	28.284	26.033		
	33.1728	28.2902	26.0866		
	33.2146	**28.2773**	**26.1139**	**27.1956**	**6.0190**
10	33.2678	26.5284	24.4353		
	33.0357	26.5434	24.1411		
	33.5971	26.517	24.2246		
	33.3002	**26.5296**	**24.267**	**25.3983**	**7.9019**

BMP-6: QRT-PCR RAW DATA

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
1	33.3769	27.6593	25.6052		
	32.8529	27.8416	25.7465		
	32.2156	27.6540	26.0428		
	32.8151	**27.7183**	**25.7982**	**26.7582**	**6.0569**
2	33.3287	27.1822	25.1020		
	33.3728	27.2291	24.8425		
	32.4526	27.0099	25.3082		
	33.0514	**27.1404**	**25.0842**	**26.1123**	**6.9391**
3	34.4713	29.0198	27.4420		
	34.7635	28.9490	27.6540		
	34.2430	28.5780	27.9448		
	34.4926	**28.8489**	**27.6803**	**28.2646**	**6.2280**
4	34.5847	26.5070	24.7654		
	35.1692	26.3552	24.5419		
	34.3095	26.4610	25.0941		
	34.6878	**26.4411**	**24.8005**	**25.6208**	**9.0670**
5	36.3237	27.1587	25.0434		
	35.8397	27.1265	25.1972		
	35.7805	26.9038	25.4906		
	35.9813	**27.0630**	**25.2437**	**26.1534**	**9.8279**
6	35.6240	29.1832	26.6170		
	34.8909	29.0685	26.5990		
	34.6864	29.0432	27.1175		
	35.0671	**29.0983**	**26.7778**	**27.9381**	**7.1290**
7	33.3170	28.1248	25.6727		
	33.1351	27.9396	25.5519		
	32.6463	27.8572	25.7414		
	33.0328	**27.9739**	**25.6553**	**26.8146**	**6.2182**
8	33.4209	28.2741	25.9266		
	32.9973	28.0849	25.6750		
	32.4202	27.9657	26.0175		
	32.9461	**28.1082**	**25.8730**	**26.9906**	**5.9555**
9	31.8832	27.6665	24.6740		
	31.9588	27.8047	25.1131		
	33.8652	28.5579	25.9627		
	31.9210	**28.0097**	**25.2499**	**26.6298**	**5.2912**
10	32.2860	26.9148	25.5679		
	32.4472	27.0924	25.3188		
	33.1164	27.5023	24.9513		
	32.6165	**27.1698**	**25.2793**	**26.2246**	**6.3920**
11	32.1539	27.8387	25.8126		
	32.1730	27.6061	25.8382		
	32.1074	27.3876	25.9478		
	32.1448	**27.6108**	**25.8662**	**26.7385**	**5.4063**
12	34.0137	28.5958	27.0511		
	33.9957	28.5322	27.0110		
	34.0467	28.6432	26.7718		
	34.0187	**28.5904**	**26.9446**	**27.7675**	**6.2512**

BMP-6: QRT-PCR RAW DATA (continued).

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
13	31.5996	27.7207	26.1265		
	31.2788	27.6130	25.9008		
	31.4264	27.5997	25.8514		
	31.4349	**27.6445**	**25.9596**	**26.8020**	**4.6329**
14	34.1309	28.0618	25.9087		
	33.7364	28.0427	25.7371		
	33.3706	27.6394	25.9714		
	33.7460	**27.9146**	**25.8724**	**26.8935**	**6.8525**

NA SAMPLE	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	32.9330	25.0994	22.6239		
	32.5535	25.1613	21.8624		
	32.4725	25.4525	22.4674		
	32.6530	**25.2377**	**22.3179**	**23.7778**	**8.8752**
2	34.0828	25.6989	23.1125		
	33.6771	25.8848	22.9083		
	33.5259	25.5091	22.9230		
	33.7619	**25.6976**	**22.9813**	**24.3394**	**9.4225**
3	33.7523	26.1569	25.1140		
	34.2473	26.1605	25.1470		
	33.4669	26.2515	25.0016		
	33.8222	**26.1896**	**25.0875**	**25.6386**	**8.1836**
4	32.4559	23.9207	21.8305		
	33.0698	23.8038	21.4178		
	32.3857	24.5730	21.4083		
	32.6371	**24.0992**	**21.5522**	**22.8257**	**9.8115**
5	32.6645	26.2694	24.3608		
	33.5413	26.4458	24.4712		
	32.5572	26.2939	24.3716		
	32.9210	**26.3364**	**24.4012**	**25.3688**	**7.5522**
6	32.7013	24.6410	22.5814		
	32.9648	25.0041	22.6435		
	32.6967	24.7671	22.7404		
	32.7876	**24.8041**	**22.6551**	**23.7296**	**9.0580**
7	30.6392	24.1397	20.8068		
	30.9124	24.1158	20.9277		
	30.3754	24.0508	20.7846		
	30.6423	**24.1021**	**20.8397**	**22.4709**	**8.1714**
8	33.8156	26.3132	24.9274		
	34.4803	26.1942	24.9541		
	34.4421	25.7688	24.5310		
	34.2460	**26.0921**	**24.8042**	**25.4481**	**8.7979**

BMP-6: QRT-PCR RAW DATA (continued).

AOD SAMPLES	C1	GAPDH C2	B actin C3	C4 = AVG (C2,C3)	C4-C1
1	35.2547	27.0278	25.2553		
	35.1348	27.0605	25.1219		
	34.6047	27.1064	25.1766		
	34.9981	**27.0649**	**25.1846**	**26.1248**	**8.8733**
2	30.8417	26.1170	24.3772		
	31.1417	26.3948	24.1835		
	31.0772	26.2598	24.1477		
	31.0202	**26.2572**	**24.2361**	**25.2467**	**5.7735**
3	33.7593	27.8454	25.6122		
	34.1084	27.7831	25.6606		
	33.5781	27.5773	25.6713		
	33.8153	**27.7353**	**25.6480**	**26.6917**	**7.1236**
4	32.6269	27.1475	25.9176		
	32.7229	26.7995	25.5791		
	32.4084	27.3582	25.4227		
	32.5861	**27.1017**	**25.6398**	**26.3708**	**6.2153**
5	32.1337	29.0031	26.4356		
	32.8466	29.1032	26.5558		
	33.2291	28.9761	26.4317		
	32.7365	**29.0275**	**26.4744**	**27.7509**	**4.9856**
6	35.0885	26.1521	24.8653		
	35.3393	26.1847	24.5956		
	35.5062	26.1819	24.4566		
	35.3113	**26.1729**	**24.6392**	**25.4060**	**9.9053**
7	31.7474	26.1315	24.1087		
	32.0205	25.9871	24.0408		
	32.0985	25.9884	23.3121		
	31.9555	**26.0357**	**23.8205**	**24.9281**	**7.0274**
8	33.8232	26.9539	25.2487		
	33.8790	26.9952	25.2379		
	34.0103	26.8781	25.3167		
	33.9042	**26.9424**	**25.2678**	**26.1051**	**7.7991**
9	33.5242	26.3098	24.5545		
	33.4330	25.9725	24.1300		
	32.9230	26.3023	24.0141		
	33.2934	**26.1949**	**24.2329**	**25.2139**	**8.0795**
10	33.1086	25.7976	23.8429		
	34.2496	25.7016	23.9169		
	34.2596	25.5096	24.0126		
	33.8726	**25.6696**	**23.9241**	**24.7969**	**9.0757**
11	33.1208	23.3543	22.1173		
	33.3223	23.4484	22.1517		
	32.7554	23.3553	22.0651		
	33.0662	**23.3860**	**22.1114**	**22.7487**	**10.3175**

CATHEPSIN H: QRT-PCR RAW DATA

AAA SAMPLE	C1	GAPDH C2	B actin C3	C4= AVG (C2,C3)	C4-C1
1	32.1765	27.5677	26.0718		
	32.3035	27.5245	25.9007		
	32.2914	27.9495	26.0044		
	32.2571	**27.6806**	**25.9923**	**26.8364**	**5.4207**
2	30.1333	26.9935	25.3750		
	30.2702	26.8731	25.1023		
	30.6574	27.0171	25.0114		
	30.3536	**26.9612**	**25.1629**	**26.0621**	**4.2916**
3	32.2251	28.5773	27.4115		
	32.2592	28.3644	27.2813		
	32.0578	28.3552	26.8337		
	32.1807	**28.4323**	**27.1755**	**27.8039**	**4.3768**
4	30.7451	26.3286	24.6993		
	30.6447	26.3604	24.5749		
	30.6146	26.2520	24.4304		
	30.6681	**26.3137**	**24.5682**	**25.4409**	**5.2272**
5	31.7582	27.0854	25.1718		
	32.3463	26.9350	25.0572		
	31.9647	27.0299	25.2590		
	32.0231	**27.0168**	**25.1627**	**26.0897**	**5.9334**
6	31.4249	29.1185	26.8822		
	31.0292	29.1031	26.9648		
	31.2196	29.0595	26.4490		
	31.2246	**29.0937**	**26.7653**	**27.9295**	**3.2951**
7	31.3377	27.9419	25.4877		
	31.3990	27.6460	25.5129		
	31.2374	27.5707	25.2917		
	31.3247	**27.7195**	**25.4308**	**26.5752**	**4.7496**
8	31.1556	27.7148	25.4925		
	31.2278	27.6111	25.2447		
	30.8716	27.8669	25.5133		
	31.0850	**27.7309**	**25.4168**	**26.5739**	**4.5111**
9	29.9187	27.2316	24.5851		
	30.4054	27.1934	24.4609		
	30.9622	27.2259	24.4616		
	30.4288	**27.2170**	**24.5025**	**25.8598**	**4.5690**
10	30.7626	26.3278	24.9281		
	30.7489	26.3707	24.8005		
	30.1710	26.7880	24.7564		
	30.5608	**26.4955**	**24.8283**	**25.6619**	**4.8989**
11	31.2668	27.5597	25.6125		
	31.2246	27.3175	25.2351		
	31.4242	27.2566	25.4791		
	31.3052	**27.3779**	**25.4422**	**26.4101**	**4.8951**
12	31.1034	29.0029	26.4184		
	32.0380	28.2559	26.5910		
	31.7457	28.5386	26.5029		
	31.6290	**28.5991**	**26.5041**	**27.5516**	**4.0774**

CATHEPSIN H: QRT-PCR RAW DATA (continued).

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
13	31.0931	27.1923	25.4714		
	31.2397	27.3273	25.6739		
	31.1834	27.1157	25.3421		
	31.1721	**27.2118**	**25.4958**	**26.3538**	**4.8183**

NA SAMPLE	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	31.6411	25.9706	23.4835		
	31.7263	25.8346	23.3397		
	31.5415	26.1397	23.5344		
	31.6363	**25.9816**	**23.4525**	**24.7171**	**6.9192**
2	34.0364	27.3143	24.9735		
	33.3296	27.4106	24.2057		
	34.0121	27.1971	24.1586		
	33.7927	**27.3073**	**24.4459**	**25.8766**	**7.9161**
3	31.0586	27.5593	26.6555		
	31.3944	27.4605	26.1938		
	31.2803	27.1992	26.1255		
	31.2444	**27.4063**	**26.3249**	**26.8656**	**4.3788**
4	31.5151	25.7583	23.4403		
	32.2523	25.9829	23.2240		
	31.9276	25.9217	23.1837		
	31.8983	**25.8876**	**23.2827**	**24.5852**	**7.3132**
5	30.7106	28.2357	26.2853		
	30.3884	28.1565	26.3186		
	30.6047	28.1425	26.2382		
	30.5679	**28.1782**	**26.2807**	**27.2295**	**3.3384**
6	31.3545	25.2697	24.1449		
	31.5907	25.1079	23.9718		
	31.3915	25.1797	23.7194		
	31.4456	**25.1858**	**23.9454**	**24.5656**	**6.8800**
7	33.2405	26.1636	24.4119		
	33.1084	26.0321	24.4153		
	32.5610	26.0519	24.4108		
	32.9700	**26.0825**	**24.4127**	**25.2476**	**7.7224**
8	32.0761	25.8905	22.5069		
	32.1226	26.1003	22.6967		
	31.9742	25.7506	22.9032		
	32.0576	**25.9138**	**22.7023**	**24.3080**	**7.7496**

CATHEPSIN H: QRT-PCR RAW DATA (continued).

AOD SAMPLES	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	32.2024	26.7055	24.9907		
	33.1191	26.6390	25.0009		
	32.5743	27.0775	25.2685		
	32.6319	**26.8073**	**25.0867**	**25.9470**	**6.6849**
2	29.5736	25.6347	23.8164		
	30.0775	25.8529	23.7452		
	30.1542	25.7206	23.8213		
	29.9351	**25.7361**	**23.7943**	**24.7652**	**5.1699**
3	33.6592	27.3599	25.5423		
	34.0097	26.8657	25.1070		
	34.3542	27.0601	25.0837		
	34.0077	**27.0952**	**25.2443**	**26.1698**	**7.8379**
4	31.1261	26.5032	24.9432		
	31.8691	26.4243	24.6651		
	31.1008	26.6964	24.6672		
	31.3653	**26.5413**	**24.7585**	**25.6499**	**5.7154**
5	30.8757	28.3628	26.4216		
	31.2599	28.4409	26.0153		
	31.9860	28.6164	26.1793		
	31.3739	**28.4734**	**26.2054**	**27.3394**	**4.0345**
6	31.6889	27.2793	25.4923		
	31.5374	27.1941	25.2531		
	31.7940	27.0541	25.1810		
	31.6734	**27.1758**	**25.3088**	**26.2423**	**5.4311**
7	30.3448	26.4675	24.5868		
	30.4135	26.6082	24.7805		
	30.4708	26.4644	24.4103		
	30.4097	**26.5134**	**24.5925**	**25.5530**	**4.8568**
8	34.2729	28.0238	25.9367		
	35.0448	28.0158	25.7734		
	35.2062	27.3428	25.7746		
	34.8413	**27.7941**	**25.8282**	**26.8112**	**8.0301**
9	31.1478	26.7196	25.2629		
	30.8827	27.0086	25.1156		
	31.0552	27.2436	25.2891		
	31.0286	**26.9906**	**25.2225**	**26.1066**	**4.9220**
10	31.7525	26.2794	24.4191		
	32.0377	26.2680	24.5213		
	32.3872	26.2891	24.9049		
	32.0591	**26.2788**	**24.6151**	**25.4470**	**6.6122**

CD79A : QRT-PCR RAW DATA

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
1	27.4110	25.5634	24.0383		
	27.2842	25.5490	23.7237		
	27.2515	26.0362	23.8222		
	27.3156	**25.7162**	**23.8614**	**24.7888**	**2.5268**
2	28.4447	25.0955	23.1873		
	28.3324	25.0406	23.1539		
	28.4366	24.9522	23.0123		
	28.4046	**25.0294**	**23.1178**	**24.0736**	**4.3309**
3	30.0250	27.0100	25.6002		
	29.6548	26.8492	25.5773		
	29.6068	26.7243	25.4295		
	29.7622	**26.8612**	**25.5357**	**26.1984**	**3.5638**
4	29.2478	24.4339	22.7899		
	29.1878	24.6258	22.7357		
	28.9259	24.6026	22.6202		
	29.1205	**24.5541**	**22.7153**	**23.6347**	**5.4858**
5	31.5081	25.1644	23.4378		
	31.7536	25.2053	23.3627		
	31.3088	25.1365	23.3334		
	31.5235	**25.1687**	**23.3780**	**24.2734**	**7.2502**
6	27.6049	27.1072	24.9013		
	27.4378	27.1433	24.8476		
	27.3520	27.0726	24.7625		
	27.4649	**27.1077**	**24.8371**	**25.9724**	**1.4925**
7	28.2369	26.0105	23.8204		
	28.0815	25.9779	23.7152		
	27.9734	25.7513	23.6585		
	28.0973	**25.9132**	**23.7314**	**24.8223**	**3.2750**
8	28.4028	25.8588	23.7512		
	28.2945	25.9313	23.5084		
	28.2570	26.0995	23.5335		
	28.3181	**25.9632**	**23.5977**	**24.7805**	**3.5377**
9	26.3837	25.2730	22.4660		
	26.3416	25.2970	22.4104		
	25.9221	25.2048	22.4879		
	26.2158	**25.2583**	**22.4548**	**23.8565**	**2.3593**
10	30.4830	25.1828	23.5611		
	30.7883	25.1764	23.5555		
	30.5551	25.2763	23.5587		
	30.6088	**25.2118**	**23.5584**	**24.3851**	**6.2237**
11	28.2440	25.8480	23.8479		
	28.3372	25.8666	23.8686		
	28.5311	25.9334	23.8875		
	28.3708	**25.8827**	**23.8680**	**24.8753**	**3.4954**
12	29.1595	27.1736	25.2426		
	29.2605	27.1692	25.2253		
	29.0401	27.1064	25.1665		
	29.1534	**27.1497**	**25.2115**	**26.1806**	**2.9728**

CD79A : QRT-PCR RAW DATA (continued).

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
13	27.2768	26.0749	23.9632		
	27.2584	26.1223	23.9384		
	27.2628	26.0029	23.7858		
	27.2660	**26.0667**	**23.8958**	**24.9813**	**2.2848**

NA SAMPLE	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	32.8447	24.5994	22.1501		
	32.4977	24.5331	22.1813		
	32.5537	24.8661	22.0615		
	32.6320	**24.6662**	**22.1310**	**23.3986**	**9.2335**
2	36.6479	25.3072	21.9562		
	34.3967	24.8114	21.9899		
	34.5092	24.4916	22.2395		
	35.1846	**24.8701**	**22.0619**	**23.4660**	**11.7186**
3	30.7098	25.1976	24.8588		
	30.7537	25.7629	24.7274		
	30.2165	25.8087	24.7149		
	30.5600	**25.5897**	**24.7670**	**25.1784**	**5.3816**
4	33.5206	23.5991	21.3484		
	33.4039	24.0255	21.3460		
	33.2923	23.6644	21.6835		
	33.4056	**23.7630**	**21.4593**	**22.6112**	**10.7945**
5	27.4477	25.7675	24.1823		
	27.4316	25.9747	24.1048		
	27.5032	25.6856	28.3577		
	27.4608	**25.8093**	**25.5483**	**25.6788**	**1.7821**
6	34.7925	22.9819	21.9909		
	34.9981	22.9278	21.5973		
	34.1916	23.0197	22.5986		
	34.6607	**22.9765**	**22.0623**	**22.5194**	**12.1414**
7	34.3082	23.6380	22.1699		
	33.9995	23.6444	22.0318		
	34.0773	23.8504	22.1269		
	34.1283	**23.7109**	**22.1095**	**22.9102**	**11.2181**
8	33.9023	23.7568	20.6021		
	35.2272	23.6767	20.6801		
	34.0219	23.8708	20.5292		
	34.3838	**23.7681**	**20.6038**	**22.1860**	**12.1979**

CD79A : QRT-PCR RAW DATA (continued).

AOD SAMPLES	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	33.3408	25.4637	23.3565		
	33.4787	25.4730	23.4268		
	33.3793	25.3681	23.5084		
	33.3996	**25.4349**	**23.4306**	**24.4328**	**8.9669**
2	27.5648	24.6939	22.3362		
	27.5034	24.6598	22.3494		
	27.5970	24.5232	22.4095		
	27.5551	**24.6256**	**22.3650**	**23.4953**	**4.0597**
3	34.7580	25.7235	23.7404		
	34.6440	25.7747	23.6813		
	34.1287	25.6110	23.7013		
	34.5102	**25.7031**	**23.7077**	**24.7054**	**9.8049**
4	28.3629	25.3451	23.7928		
	28.4720	25.5467	23.4206		
	28.4226	25.5069	23.2506		
	28.4192	**25.4662**	**23.4880**	**24.4771**	**3.9421**
5	28.1895	27.3443	25.1256		
	28.1386	27.4329	24.5166		
	27.6970	27.5032	24.7254		
	28.0084	**27.4268**	**24.7892**	**26.1080**	**1.9004**
6	37.0674	25.6428	24.3021		
	35.9405	25.3436	24.3966		
	38.6284	25.8219	24.0812		
	37.2121	**25.6028**	**24.2600**	**24.9314**	**12.2807**
7	30.2919	25.3771	24.0618		
	30.0981	25.1514	22.9435		
	30.2307	25.2074	23.2181		
	30.2069	**25.2453**	**23.4078**	**24.3266**	**5.8804**
8	36.9228	26.3388	24.8060		
	34.8010	26.4489	24.5600		
	33.8072	26.2013	24.6320		
	35.1770	**26.3297**	**24.6660**	**25.4978**	**9.6792**
9	29.0222	25.4770	24.0079		
	28.9405	25.5263	23.6848		
	29.0183	26.0122	23.5497		
	28.9937	**25.6718**	**23.7475**	**24.7097**	**4.2840**
10	30.7327	25.1709	23.1202		
	32.3256	25.3002	23.1011		
	32.1583	25.3010	23.1117		
	31.7389	**25.2574**	**23.1110**	**24.1842**	**7.5547**

MMP9: QRT-PCR RAW DATA

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
1	29.9616	28.6521	26.7632		
	30.0633	28.5121	26.6328		
	29.4765	28.4414	26.9396		
	29.8338	**28.5352**	**26.7785**	**27.6569**	**2.1769**
2	28.8515	29.0148	26.8070		
	28.8330	28.8926	26.8848		
	28.8526	28.8633	26.7901		
	28.8457	**28.9236**	**26.8273**	**27.8754**	**0.9703**
3	32.1521	24.8204	23.4856		
	31.8337	24.7073	23.4596		
	31.3724	24.7926	28.1650		
	31.7861	**24.7734**	**23.4726**	**24.1230**	**7.6631**
4	36.2558	27.2579	25.6928		
	34.7953	27.2378	25.6339		
	35.8870	27.2451	25.5789		
	35.3412	**27.2469**	**25.6352**	**26.4411**	**8.9001**
5	38.2055	25.9296	24.3822		
	37.7348	25.9031	24.1271		
	37.7348	26.1617	23.9325		
	37.8917	**25.9981**	**24.1473**	**25.0727**	**12.8190**
6	27.3843	27.5262	25.5412		
	27.2650	27.5340	25.4284		
	27.2435	28.0469	25.4493		
	27.2976		**25.4730**	**25.4730**	**1.8246**
7	30.7445	27.5421	25.6863		
	30.2088	27.4953	25.5135		
	30.4542	27.4999	25.3794		
	30.4692	**27.5124**	**25.5264**	**26.5194**	**3.9498**
8	27.3179	26.3867	24.6477		
	27.2870	26.2916	24.5447		
	27.1412	26.2222	24.3715		
	27.2487	**26.3002**	**24.5213**	**25.4107**	**1.8380**
9	28.4699	27.2075	24.7146		
	28.2575	27.1585	24.4922		
	28.1549	27.1179	24.4905		
	28.2941	**27.1613**	**24.5658**	**25.8635**	**2.4306**
10	29.0540	26.3859	25.1314		
	28.8105	26.5170	25.0433		
	29.0016	26.4833	24.9516		
	28.9554	**26.4621**	**25.0421**	**25.7521**	**3.2033**
11	30.7197	27.5651	25.1634		
	30.4710	27.4874	25.2170		
	30.4844	27.4077	25.1333		
	30.5584	**27.4867**	**25.1712**	**26.3290**	**4.2294**
12	26.7280	27.0240	25.7541		
	26.7278	27.0702	25.3158		
	26.7327	27.0965	25.7376		
	26.7295	**27.0636**	**25.6025**	**25.6025**	**1.1270**

MMP9: QRT-PCR RAW DATA (continued).

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
13	31.0333	28.4445	27.2998		
	30.9748	28.5254	27.1004		
	31.2917	28.8975	27.2292		
	31.0999	**28.6225**	**27.2098**	**27.9161**	**3.1838**

NA SAMPLE	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	31.1668	25.4162	23.2758		
	31.0349	25.4247	23.2196		
	31.5223	25.4656	23.2038		
	31.2413	**25.4355**	**23.2331**	**24.3343**	**6.9071**
2	32.4260	25.1529	23.8821		
	32.1697	25.0815	23.8409		
	31.7569	25.1333	28.5185		
	32.1175	**25.1226**	**23.8615**	**24.4920**	**7.6255**
3	38.5511	26.2374	24.7679		
	38.1593	26.2242	24.4476		
	38.1593	26.4846	24.2884		
	38.2899	**26.3154**	**24.5013**	**25.4084**	**12.8816**
4	29.6525	26.7882	24.5879		
	29.5438	26.7402	24.4848		
	29.3985	27.2087	24.4583		
	29.5316	**26.9124**	**24.5103**	**25.7114**	**3.8202**
5	30.8313	25.1124	22.9688		
	30.6340	25.1171	22.8925		
	31.2055	25.1539	22.8935		
	30.8903	**25.1278**	**22.9183**	**24.0230**	**6.8672**
6	30.1208	26.2171	24.2982		
	29.6311	26.1258	24.2087		
	29.7360	26.0188	24.1703		
	29.8293	**26.1206**	**24.2257**	**25.1732**	**4.6562**
7	29.6126	28.3046	26.3944		
	29.7059	28.1697	26.2962		
	29.1714	28.1131	26.5499		
	29.4966	**28.1958**	**26.4135**	**27.3047**	**2.1920**
8	30.6871	27.3177	26.1519		
	30.7233	27.3250	26.0401		
	30.5108	27.8252	26.0562		
	30.6404	**27.4893**	**26.0827**	**26.7860**	**3.8544**
9	34.2093	25.9396	23.1753		
	33.6651	25.5703	23.2647		
	33.3931	25.5590	23.1740		
	33.7558	**25.6896**	**23.2047**	**24.4472**	**9.3087**

MMP9: QRT-PCR RAW DATA (continued).

AOD SAMPLES	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	30.0244	27.1300	25.0167		
	29.9671	27.0993	24.8779		
	29.7297	27.5322	24.8455		
	29.9071	**27.2538**	**24.9134**	**26.0836**	**3.8235**
2	30.3591	26.5377	24.6547		
	30.0025	26.4232	24.5475		
	30.0785	26.3049	24.4900		
	30.1467	**26.4219**	**24.5641**	**25.4930**	**4.6537**
3	36.6088	27.5981	26.0766		
	35.2018	27.5764	26.0332		
	36.2866	27.5931	25.9760		
	36.0324	**27.5892**	**26.0286**	**26.8089**	**9.2235**
4	29.4164	28.7575	26.3730		
	29.1878	28.9048	26.2536		
	29.4437	28.8453	26.5427		
	29.3493	**28.8359**	**26.3898**	**27.6128**	**1.7365**
5	28.5286	28.6027	26.4395		
	28.4998	28.4752	26.5076		
	28.5233	28.4513	26.4406		
	28.5172	**28.5097**	**26.4626**	**27.4862**	**1.0311**
6	29.1329	28.3852	26.0793		
	28.8832	28.5131	25.9488		
	29.1233	28.4537	26.2020		
	29.0465	**28.4507**	**26.0767**	**27.2637**	**1.7828**
7	31.7986	26.9358	25.0850		
	32.3130	26.8003	25.0177		
	31.6874	26.9203	25.0540		
	31.9330	**26.8855**	**25.0522**	**25.9689**	**5.9642**
8	30.5458	25.8682	24.0209		
	30.4579	25.8426	23.8165		
	30.5262	25.8109	23.7707		
	30.5100	**25.8406**	**23.8694**	**24.8550**	**5.6550**
9	28.5660	26.2307	24.6721		
	29.0274	26.4279	24.6558		
	28.5130	26.4525	24.6475		
	28.7021	**26.3704**	**24.6585**	**25.5144**	**3.1877**
10	28.8364	26.9389	25.2421		
	29.0215	26.4592	25.2680		
	28.8173	27.1941	25.1792		
	28.8917	**26.8641**	**25.2298**	**26.0469**	**2.8448**

MMP3 : QRT-PCR RAW DATA

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
1	36.7902	25.8874	24.0284		
	35.2824	25.8608	23.8609		
	34.8027	26.1203	23.9767		
	35.0426	**25.9562**	**23.9553**	**24.9558**	**10.0868**
2	33.5384	25.1223	23.4776		
	33.6037	25.1947	23.3337		
	33.8400	25.2349	23.4793		
	33.6607	**25.1840**	**23.4302**	**24.3071**	**9.3536**
3	34.3269	27.2618	25.9715		
	34.3846	27.3607	26.0657		
	33.5651	27.1382	26.0692		
	34.0922	**27.2536**	**26.0355**	**26.6445**	**7.4477**
4	34.0512	24.9406	22.9395		
	33.2909	25.0880	23.0095		
	33.4770	25.0080	23.2440		
	33.6064	**25.0122**	**23.0643**	**24.0383**	**9.5681**
5	37.8807	25.4350	23.6169		
	37.8000	25.5528	23.5379		
	45.2594	25.3876	23.6239		
	37.8000	**25.4585**	**23.5929**	**24.5257**	**13.2743**
6	36.7953	27.5016	25.1796		
	36.7953	27.5386	25.0429		
	36.7953	27.3941	24.9038		
	36.7953	**27.4781**	**25.0421**	**26.2601**	**10.5352**
7	40.4999	26.1166	23.7698		
	40.4999	26.0456	23.8250		
	40.4999	26.0703	24.0358		
	40.4999	**26.0775**	**23.8769**	**24.9772**	**15.5227**
8	33.9614	26.1066	23.8967		
	34.3082	26.1342	23.9155		
	34.3671	26.1813	24.2142		
	34.2122	**26.1407**	**24.0088**	**25.0748**	**9.1375**
9	36.0579	25.7443	23.0291		
	36.0970	25.7799	23.4775		
	35.3753	**25.8566**	**22.8996**	**24.3781**	**10.9972**
10	33.0504	25.5164	24.1759		
	33.0161	25.6059	24.0309		
	33.4348	26.1323	24.0785		
	33.1671	**25.7515**	**24.0951**	**24.9233**	**8.2438**
11	36.9704	26.1947	24.2380		
	39.1457	26.1317	24.2797		
	37.3352	26.2173	24.1705		
	37.8171	**26.1812**	**24.2294**	**25.2053**	**12.6118**
12	36.9704	27.6850	25.5664		
	36.9704	27.7683	25.6873		
	36.9704	27.5219	25.5704		
	36.9704	**27.6584**	**25.6080**	**26.6332**	**10.3372**

MMP3: QRT-PCR RAW DATA (continued).

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
13	34.9535	26.2764	24.5588		
	34.0473	26.2345	24.7169		
	33.6571	26.2144	24.2220		
	34.2193	**26.2418**	**24.4992**	**25.3705**	**8.8488**

NA SAMPLE	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	46.8864	25.2567	22.6496		
	46.8864	25.1551	22.6218		
	46.8864	25.0051	22.5083		
	46.8864	**25.1390**	**22.5932**	**23.8661**	**23.0203**
2	38.2252	25.8957	24.6796		
	38.2252	25.8906	24.7360		
	38.2252	25.8215	24.9124		
	38.2252	**25.8693**	**24.7760**	**25.3226**	**12.9026**
3	42.3070	25.2567	22.6496		
	42.6750	25.1551	22.6218		
	42.0750	25.0051	22.5083		
	42.3523	**25.1390**	**22.5932**	**23.8661**	**18.4862**
4	39.0129	24.4271	22.1194		
	38.9488	24.1875	22.0503		
	36.9929	24.7712	22.0307		
	38.3182	**24.4619**	**22.0668**	**23.2644**	**15.0538**
5	38.0517	26.8602	24.8873		
	38.9957	26.9421	25.0133		
	36.1207	26.6347	24.8055		
	37.7227	**26.8123**	**24.9020**	**25.8572**	**11.8655**
6	38.0517	23.9782	22.4725		
	38.9957	23.8451	22.4570		
	36.1207	23.7878	22.4709		
	37.7227	**23.8704**	**22.4668**	**23.1686**	**14.5541**
7	38.0375	25.0769	23.2544		
	38.0375	25.1609	22.9698		
	38.0375	25.0551	22.8998		
	38.0375	**25.0976**	**23.0413**	**24.0695**	**13.9680**
8	39.0129	24.5236	21.1595		
	39.0129	24.5058	21.1539		
	39.0129	24.4660	21.3574		
	39.0129	**24.4985**	**21.2236**	**22.8610**	**16.1519**

MMP3: QRT-PCR RAW DATA (continued).

AOD SAMPLES	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	49.1274	25.6805	23.7331		
	49.1274	25.7288	23.6539		
	49.1274	25.5296	23.7872		
	49.1274	**25.6463**	**23.7247**	**24.6855**	**24.4419**
2	31.4277	24.8132	22.9353		
	31.2524	24.6855	22.6292		
	31.0605	24.7966	22.5422		
	31.2469	**24.7651**	**22.7022**	**23.7337**	**7.5132**
3	47.9726	26.1328	24.3299		
	44.2159	26.0626	24.2517		
	44.2159	25.9597	24.1868		
	45.4681	**26.0517**	**24.2561**	**25.1539**	**20.3142**
4	37.9100	25.9402	24.0498		
	37.9100	25.6489	23.8038		
	37.9100	25.6110	24.2222		
	37.9100	**25.7334**	**24.0253**	**24.8793**	**13.0307**
5	47.9726	27.3755	25.1594		
	44.2159	27.3261	25.2872		
	44.2159	27.5127	25.4874		
	45.4681	**27.4048**	**25.3113**	**26.3581**	**19.1101**
6	37.4631	24.9148	22.2381		
	37.4631	24.4816	22.2795		
	37.4631	24.9737	22.1915		
	37.4631	**24.7900**	**22.2364**	**23.5132**	**13.9499**
7	38.3659	26.0291	24.3783		
	38.3659	26.0779	24.2879		
	38.3659	25.9033	24.2295		
	38.3659	**26.0034**	**24.2986**	**25.1510**	**13.2149**
8	34.1710	25.5466	23.4690		
	34.6147	25.4396	24.0542		
	34.3382	25.1685	23.3524		
	34.3746	**25.3849**	**23.6252**	**24.5051**	**9.8696**
9	44.4763	26.3847	25.0254		
	44.4763	26.3911	24.7225		
	44.4763	26.1810	24.8842		
	44.4763	**26.3189**	**24.8774**	**25.5982**	**18.8782**
10	35.7865	26.0648	23.8488		
	36.4678	25.3926	23.6132		
	35.3236	25.7177	23.8922		
	35.8593	**25.7250**	**23.7847**	**24.7549**	**11.1044**
11	35.4743	25.2077	23.1854		
	36.7317	25.1428	23.1937		
	36.9200	25.2345	23.2848		
	36.3753	**25.1950**	**23.2213**	**24.2082**	**12.1672**

CD19: QRT-PCR RAW DATA

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
1	35.7633	28.4319	27.6026		
	35.9184	28.2965	27.3895		
	35.2004	28.5638	27.3408		
	35.6274	**28.4307**	**27.4443**	**27.9375**	**7.6899**
2	32.7659	27.7650	26.0795		
	32.5739	27.7673	26.1147		
	32.2767	27.8539	26.0022		
	32.5388	**27.7954**	**26.0655**	**26.9304**	**5.6084**
3	31.0860	27.0904	24.6777		
	31.0256	27.2074	24.6561		
	30.8064	27.1066	24.5926		
	30.9727	**27.1348**	**24.6421**	**25.8885**	**5.0842**
4	33.1896	28.0354	25.6511		
	33.3202	28.0519	25.5826		
	32.9914	28.4614	25.6759		
	33.1671	**28.1829**	**25.6365**	**26.9097**	**6.2574**
5	33.7839	27.1304	25.1165		
	33.2664	26.9483	25.2221		
	32.7599	27.1204	24.8725		
	33.2701	**27.0664**	**25.0704**	**26.0684**	**7.2017**
6	35.0054	26.3293	24.6715		
	35.5947	26.3202	24.5787		
	35.0803	26.4001	24.7395		
	35.2268	**26.3499**	**24.6632**	**25.5066**	**9.7203**
7	35.2966	26.9475	25.1279		
	36.0940	26.7891	25.3502		
	35.2966	26.9565	25.1279		
	35.5624	**26.8977**	**25.2020**	**26.0499**	**9.5126**
8	31.3397	27.1519	25.3154		
	31.3283	27.2454	25.4251		
	31.0220	26.7775	25.0983		
	31.2300	**27.0583**	**25.2796**	**26.1689**	**5.0611**
9	33.4245	27.5148	24.8478		
	32.9268	27.4644	24.9765		
	33.8681	27.1018	25.0425		
	33.4065	**27.3603**	**24.9556**	**26.1580**	**7.2485**
10	32.0758	27.2562	25.2722		
	32.2228	27.5099	25.2919		
	32.3863	27.1620	25.5192		
	32.2283	**27.3094**	**25.3611**	**26.3352**	**5.8931**
11	35.3117	27.0382	24.9496		
	34.5465	26.9072	24.9429		
	34.5465	27.1699	25.0990		
	34.8016	**27.0384**	**24.9972**	**26.0178**	**8.7838**
12	31.5040	28.2997	26.6795		
	31.7726	28.1369	26.6778		
	31.3745	28.1474	26.4569		
	31.5504	**28.1947**	**26.6047**	**27.3997**	**4.1507**

CD19: QRT-PCR RAW DATA (continued).

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
13	31.1543	28.6230	26.2193		
	31.3023	28.8234	26.1310		
	31.5816	28.8059	26.4912		
	31.3461	**28.7508**	**26.2805**	**27.5156**	**3.8304**

NA SAMPLE	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	34.3308	27.6046	26.1575		
	34.5822	27.5601	26.2102		
	34.5438	27.3337	26.1864		
	34.4856	**27.4995**	**26.1847**	**26.8421**	**7.6435**
2	38.4960	26.0240	23.5627		
	38.4960	26.0304	23.5545		
	38.4960	26.1835	23.7382		
	38.4960	**26.0793**	**23.6185**	**24.8489**	**13.6471**
3	38.4960	26.2206	22.8729		
	38.4960	26.1500	22.8269		
	38.4960	26.5519	22.9846		
	38.4960	**26.3075**	**22.8948**	**24.6012**	**13.8949**
4	42.1795	26.9943	24.2702		
	42.1795	27.1083	24.2679		
	42.1795	26.8830	24.2085		
	42.1795	**26.9952**	**24.2489**	**25.6220**	**16.5575**
5	31.2403	28.2333	26.6507		
	31.6789	28.2369	26.4499		
	31.5812	28.3881	26.9866		
	31.5001	**28.2861**	**26.6957**	**27.4909**	**4.0092**
6	47.6992	25.0788	23.6566		
	47.6992	24.8282	23.7371		
	47.6992	24.6575	23.8089		
	47.6992	**24.8548**	**23.7342**	**24.2945**	**23.4047**
7	41.7809	26.0027	23.9830		
	36.3397	25.8038	23.8678		
	41.7809	25.7543	23.7932		
	39.9672	**25.8536**	**23.8813**	**24.8675**	**15.0997**
8	42.1795	25.5298	23.5991		
	42.1795	25.3398	23.1623		
	42.1795	25.8638	23.0803		
	42.1795	**25.5778**	**23.2806**	**24.4292**	**17.7503**

CD19: QRT-PCR RAW DATA (continued).

AOD SAMPLES	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	34.3144	26.1822	24.3429		
	34.3279	26.2076	24.1808		
	33.5463	26.2824	24.2147		
	34.0629	**26.2241**	**24.2461**	**25.2351**	**8.8278**
2	41.0127	27.2518	25.4259		
	42.1123	27.1992	25.3500		
	40.4973	27.1674	25.4565		
	41.2074	**27.2061**	**25.4108**	**26.3085**	**14.8990**
3	32.4501	26.6211	25.0333		
	33.4156	26.7027	25.0046		
	32.7001	25.9259	24.9910		
	32.8553	**26.4166**	**25.0096**	**25.7131**	**7.1422**
4	38.0093	27.4130	26.0877		
	38.0093	27.0736	25.4659		
	38.0093	27.2763	25.7855		
	38.0093	**27.2543**	**25.7797**	**26.5170**	**11.4923**
5	39.7602	26.3840	24.5802		
	39.7602	26.4055	24.4639		
	39.7602	26.2823	24.4355		
	39.7602	**26.3573**	**24.4932**	**25.4252**	**14.3350**
6	46.1954	27.0021	25.0308		
	42.3772	27.0370	25.2744		
	42.3772	26.7400	25.1394		
	42.3772	**26.9264**	**25.1482**	**26.0373**	**16.3399**
7	31.0948	28.4033	25.7812		
	31.4516	28.4199	26.0650		
	31.4278	28.3341	26.1449		
	31.3247	**28.3858**	**25.9970**	**27.1914**	**4.1333**
8	31.2661	26.5156	24.5983		
	31.5752	26.3625	24.5847		
	31.4059	26.3999	24.6110		
	31.4157	**26.4260**	**24.5980**	**25.5120**	**5.9037**
9	36.0828	26.0978	24.1365		
	36.0828	26.0292	24.1320		
	36.0828	26.0352	24.0898		
	36.0828	**26.0541**	**24.1194**	**25.0868**	**10.9961**
10	42.4981	27.3937	25.9776		
	42.4981	27.5727	26.0415		
	42.4981	27.7603	26.1770		
	42.4981	**27.5756**	**26.0654**	**26.8205**	**15.6776**

SPEG: QRT-PCR RAW DATA

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
1	34.8003	29.0358	27.1946		
	34.8761	28.7090	27.1355		
	35.1314	28.7059	27.0866		
	34.9359	**28.8169**	**27.1389**	**27.9779**	**6.9580**
2	37.8347	29.2697	26.9635		
	37.8734	29.1488	26.8766		
	38.1624	29.1228	26.8891		
	37.9568	**29.1804**	**26.9097**	**28.0451**	**9.9117**
3	34.9066	27.1976	25.3413		
	36.6187	27.3618	24.8117		
	35.3758	27.3390	25.2552		
	35.6337	**27.2995**	**25.1361**	**26.2178**	**9.4159**
4	36.0813	27.8186	26.0042		
	36.8950	28.2825	25.9001		
	35.2944	27.6811	25.9071		
	36.0902	**27.9274**	**25.9371**	**26.9323**	**9.1580**
5	35.2873	27.9151	25.5014		
	34.4574	27.6836	25.5424		
	34.8213	27.6298	25.5308		
	34.8553	**27.7428**	**25.5249**	**26.6339**	**8.2215**
6	36.5730	29.0547	27.9082		
	38.1038	28.8943	27.7715		
	37.1168	29.2254	27.6364		
	37.2645	**29.0581**	**27.7720**	**28.4151**	**8.8495**
7	34.6980	27.3737	24.9514		
	34.8518	27.4685	24.7947		
	33.7768	27.4597	24.6656		
	34.4422	**27.4340**	**24.8039**	**26.1189**	**8.3233**
8	35.5089	26.3576	24.2671		
	35.0727	25.4188	24.4432		
	34.9770	26.3143	24.3613		
	35.1862	**26.0302**	**24.3572**	**25.1937**	**9.9925**
9	31.4317	26.7392	24.7749		
	32.2018	25.6758	24.6549		
	31.3693	26.4596	24.7644		
	31.6676	**26.2915**	**24.7314**	**25.5115**	**6.1561**
10	34.0312	27.5636	25.6476		
	33.7233	27.3518	25.3040		
	33.6727	27.4649	25.2137		
	33.8091	**27.4601**	**25.3884**	**26.4243**	**7.3848**
11	35.0267	26.3134	25.2159		
	37.5269	27.2873	25.2212		
	34.9496	27.3573	25.2647		
	35.8344	**26.9860**	**25.2339**	**26.1100**	**9.7244**
12	34.1888	27.0941	25.2764		
	34.1538	26.7225	25.2758		
	34.6669	26.8552	25.1617		
	34.3365	**26.8906**	**25.2380**	**26.0643**	**8.2722**

SPEG: QRT-PCR RAW DATA (continued)

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
13	34.8702	27.0941	25.6683		
	35.0979	27.0753	25.5907		
	34.4038	27.0096	25.8607		
	34.7906	**27.0597**	**25.7066**	**26.3831**	**8.4075**

NA SAMPLE	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	31.7500	25.2925	24.2226		
	31.5333	25.1852	24.1546		
	31.1940	25.2910	23.9760		
	31.4924	**25.2562**	**24.1177**	**24.6870**	**6.8055**
2	31.3285	26.4204	24.6258		
	31.4752	26.3336	24.4400		
	31.3661	26.3891	24.4012		
	31.3899	**26.3810**	**24.4890**	**25.4350**	**5.9549**
3	31.3014	26.0619	23.7883		
	31.5422	26.0331	23.5892		
	31.3360	25.9758	23.7142		
	31.3932	**26.0236**	**23.6972**	**24.8604**	**6.5328**
4	31.1128	26.0603	22.7446		
	31.1528	26.0016	22.7234		
	31.1067	25.9835	22.6203		
	31.1241	**26.0151**	**22.6961**	**24.3556**	**6.7685**
5	32.2156	26.9411	24.2319		
	31.6660	26.6585	24.0387		
	31.6616	26.4735	24.0024		
	31.8477	**26.6910**	**24.0910**	**25.3910**	**6.4567**
6	30.2094	25.4841	23.0783		
	29.8053	25.3182	23.0164		
	29.9297	25.3228	23.1185		
	29.9815	**25.3750**	**23.0711**	**24.2231**	**5.7584**
7	34.1377	28.6696	26.8438		
	33.4634	28.4810	26.1362		
	33.6184	28.5988	26.6796		
	33.7398	**28.5831**	**26.5532**	**27.5682**	**6.1717**
8	34.1039	27.7382	26.8042		
	34.5060	27.6652	26.6331		
	34.0113	27.7436	26.5311		
	34.2071	**27.7157**	**26.6561**	**27.1859**	**7.0212**

SPEG: QRT-PCR RAW DATA (continued).

AOD SAMPLES	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	38.2654	29.0966	26.7265		
	37.5607	28.9370	26.6802		
	37.1478	28.9877	26.7296		
	37.6580	**29.0071**	**26.7121**	**27.8596**	**9.7984**
2	32.1747	27.3036	25.2624		
	32.6829	27.3543	25.3248		
	31.9180	27.0563	25.1720		
	32.2585	**27.2381**	**25.2531**	**26.2456**	**6.0130**
3	32.8993	26.8596	24.8204		
	32.9997	26.6325	24.8656		
	33.1578	26.5424	24.6184		
	33.0189	**26.6782**	**24.7681**	**25.7232**	**7.2958**
4	31.9668	27.9780	26.1616		
	32.1331	27.9244	26.1132		
	32.2954	27.9237	26.3324		
	32.1318	**27.9420**	**26.2024**	**27.0722**	**5.0596**
5	33.1789	26.6141	25.0782		
	32.8269	26.6485	24.9289		
	32.5048	26.7061	24.9565		
	32.8369	**26.6562**	**24.9879**	**25.8221**	**7.0148**
6	35.2614	26.1334	24.1274		
	35.9655	26.0578	24.0327		
	35.1410	26.0277	24.0843		
	35.4560	**26.0730**	**24.0815**	**25.0772**	**10.3788**
7	31.1284	26.4501	24.6817		
	30.8563	26.5243	24.4570		
	30.8002	26.7515	24.8311		
	30.9283	**26.5753**	**24.6566**	**25.6160**	**5.3124**
8	32.7470	26.9116	25.1337		
	32.7091	26.0148	25.1516		
	33.0543	26.6437	25.0136		
	32.8368	**26.5234**	**25.0996**	**25.8115**	**7.0253**
9	32.3550	26.6946	24.9810		
	32.1150	25.8308	25.0704		
	31.9596	26.8524	24.8405		
	32.1432	**26.4593**	**24.9640**	**25.7116**	**6.4316**
10	34.7589	27.6640	26.3404		
	34.8251	27.7343	25.9992		
	33.8867	27.8043	26.2559		
	34.4902	**27.7342**	**26.1985**	**26.9664**	**7.5239**

SPIB TRANSCRIPTION FACTOR: QRT-PCR RAW DATA

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
1	31.3549	25.8814	24.0881		
	31.4873	26.0554	24.0677		
	31.4095	26.2949	23.8386		
	31.4172	26.0772	23.9981	**25.0377**	**6.3796**
2	29.3341	25.7907	22.8349		
	29.3790	25.6801	22.9250		
	29.0753	25.6937	22.9767		
	29.2628	25.7215	**22.9122**	24.3169	**4.9460**
3	32.2067	25.4784	23.4058		
	31.7074	25.2970	23.6058		
	32.1434	25.3190	23.4210		
	32.0192	**25.3648**	**23.4775**	**24.4212**	**7.5980**
4	33.3928	24.8086	22.9848		
	33.3330	24.8463	23.3688		
	33.4071	24.8259	23.0171		
	33.3776	**24.8269**	**23.1236**	**23.9753**	**9.4024**
5	35.0918	25.5146	23.6060		
	35.0830	25.3623	23.6131		
	35.3277	25.3152	23.5152		
	35.1675	**25.3974**	**23.5781**	**24.4877**	**10.6798**
6	30.7004	27.8090	25.1834		
	30.2421	27.4701	25.1015		
	30.2086	27.4253	24.9091		
	30.3837	**27.5681**	**25.0647**	**26.3164**	**4.0673**
7	31.7388	26.2894	23.9553		
	31.8016	26.3291	24.1011		
	31.6892	26.2539	24.1853		
	31.7432	**26.2908**	**24.0806**	**25.1857**	**6.5575**
8	34.8818	27.2421	25.8951		
	34.4308	27.1881	25.9917		
	34.2326	27.1423	25.7438		
	34.5151	**27.1908**	**25.8769**	**26.5339**	**7.9812**
9	33.6722	26.4120	24.4442		
	33.7260	26.3752	23.9885		
	33.5224	26.5257	24.2377		
	33.6402	**26.4376**	**24.2235**	**25.3306**	**8.3097**
10	35.3859	25.2894	23.8495		
	35.3313	25.1800	23.9652		
	35.1728	25.5695	23.9601		
	35.2967	**25.3463**	**23.9249**	**24.6356**	**10.6611**
11	32.6332	26.0154	24.1791		
	32.4925	26.0655	24.1914		
	32.3316	25.8232	24.0386		
	32.4858	**25.9680**	**24.1364**	**25.0522**	**7.4336**
12	31.8322	27.2560	25.3137		
	31.8335	27.0635	25.3436		
	31.6735	27.0005	25.2226		
	31.7797	**27.1067**	**25.2933**	**26.2000**	**5.5798**

SPIB TRANSCRIPTION FACTOR: QRT-PCR RAW DATA (continued).

AAA SAMPLE	C1	GAPDH C2	Bactin C3	C4= AVG (C2,C3)	C4-C1
13	31.9408	26.1412	24.3549		
	31.9001	26.1443	24.2187		
	32.1484	26.1359	24.1406		
	31.9964	**26.1405**	**24.2381**	**25.1893**	**6.8072**

NA SAMPLE	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	34.3453	24.2611	21.6710		
	34.4124	24.2572	21.7770		
	34.4124	24.5708	21.8864		
	34.3900	**24.3630**	**21.7781**	**23.0706**	**11.3195**
2	38.9587	24.7442	22.1514		
	37.8992	24.7453	22.1217		
	38.4290	24.7780	22.0236		
	38.1641	**24.7558**	**22.0989**	**23.4274**	**14.7367**
3	39.0313	23.9333	21.6989		
	38.0470	24.0378	21.6184		
	38.5392	24.3170	21.6023		
	38.5392	**24.0960**	**21.6399**	**22.8680**	**15.6712**
4	30.1151	26.3926	24.4379		
	30.1162	26.3217	24.4285		
	30.1146	26.3834	24.3220		
	30.1153	**26.3659**	**24.3961**	**25.3810**	**4.7343**
5	38.2665	23.3614	21.7739		
	37.5670	23.2764	22.0809		
	37.0595	23.4821	21.8935		
	37.6310	**23.3733**	**21.9161**	**22.6447**	**14.9863**
6	36.5005	24.2178	22.2232		
	38.9081	24.4219	22.6696		
	37.9127	24.1970	22.2689		
	37.7738	**24.2789**	**22.3872**	**23.3331**	**14.4407**
7	36.2506	25.2585	21.0277		
	36.8617	25.2219	20.7942		
	36.1132	24.3376	20.9309		
	36.4085	**24.9393**	**20.9176**	**22.9285**	**13.4800**

SPIB TRANSCRIPTION FACTOR: QRT-PCR RAW DATA (continued)

AOD SAMPLES	C1	GAPDH C2	Bactin C3	C4 = AVG (C2,C3)	C4-C1
1	30.5982	27.2435	24.8015		
	30.6213	27.5036	25.0067		
	30.6477	27.6166	25.0182		
	30.6224	**27.4546**	**24.9421**	**26.1984**	**4.4241**
2	35.4631	25.4467	23.8600		
	37.0471	25.5804	23.7695		
	36.5378	25.5889	23.8101		
	36.3493	**25.5387**	**23.8132**	**24.6759**	**11.6734**
3	31.6634	24.8765	22.4171		
	31.9341	25.0721	22.7484		
	31.8763	24.4112	22.6837		
	31.8246	**24.7866**	**22.6164**	**23.7015**	**8.1231**
4	44.0526	26.0825	24.0663		
	44.7060	26.0778	24.0275		
	44.3793	25.8421	23.9488		
	44.3793	**26.0008**	**24.0142**	**25.0075**	**19.3718**
5	32.0017	25.9040	23.6104		
	31.8062	25.6222	23.5892		
	32.1376	25.5247	23.9225		
	31.9818	**25.6836**	**23.7074**	**24.6955**	**8.2745**
6	31.5699	25.1009	22.7640		
	31.5699	25.2903	22.7640		
	31.5699	25.4672	22.7640		
	31.5699	**25.2861**	**22.7640**	**24.0251**	**7.5448**
7	36.6355	25.6622	23.8827		
	37.9414	25.7820	23.8596		
	37.2885	25.6470	23.7899		
	37.6149	**25.6971**	**23.8441**	24.7706	**12.8444**
8	33.2784	24.8962	22.6666		
	33.7799	25.0330	22.8651		
	33.5292	24.9191	22.6706		
	33.6545	**24.9494**	**22.7341**	**23.8418**	**9.8128**
9	38.5343	25.9529	23.8954		
	46.6118	26.1724	24.1860		
	42.5731	26.3128	24.0407		
	42.5731	**26.1460**	**24.0407**	**25.0934**	**17.4797**
10	36.0111	24.6898	23.2818		
	37.4123	24.9680	22.9656		
	36.7117	25.2015	23.1237		
	36.7117	**24.9531**	**23.1237**	**24.0384**	**12.6733**